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APPROACHES TO DISCONTINUING EFALIZUMAB: AN OPEN-LABEL STUDY OF THERAPIES FOR MANAGING INFLAMMATORY RECURRENCE

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Efalizumab is a humanised recombinant monoclonal IgG1 antibody for the treatment of moderate-to-severe plaque psoriasis. When treatment discontinuation is necessary, however, some patients may experience inflammatory recurrence of the disease, which can progress to rebound if untreated. This analysis evaluated approaches for managing inflammatory recurrence after discontinuation of efalizumab.

Background

Psoriasis is an inflammatory skin disorder that affects approximately 2–3% of the population [1] and has a profound impact on quality of life, equivalent to that of other major diseases [2]. Patients with the disease present with well-defined, thickened erythematous patches, typically covered with a silver scale, and the condition is characterized by epidermal hyperplasia, dermal angiogenesis, infiltration of activated T-cells and increased cytokine levels [3]. Chronic psoriasis is a condition requiring long-term medication. Systemic therapies are required by patients with moderate-to-severe disease; a variety of systemic therapies are available, but many of the current agents have serious side-effects that limit long-term administration [4,5].

The aetiology and pathology of psoriasis are not wellunderstood, but it has been established that T-cells are centrally involved in its development [3]. Recent understanding of the inflammatory pathways in psoriasis has led to the development and use of new biologic agents to treat the condition. One such biologic therapy, efalizumab, is a humanised recombinant monoclonal IgG1 antibody. Efalizumab binds to the alpha-subunit, CD11a, of the T-cell adhesion molecule, leukocyte function-associated antigen-1 (LFA-1), preventing binding with its ligand, intercellular adhesion molecule-1 (ICAM-1), on target cells. This action blocks several T-cell processes important in the pathogenesis of psoriasis, including Tcell activation, T-cell trafficking from the circulation into the skin, and T-cell reactivation in the dermis and epidermis [3,6,7].

Several large clinical studies have established the safety and efficacy of efalizumab during extended treatment of patients with moderate-to-severe chronic plaque psoriasis [8-10]. There are occasions, however, such as during pregnancy or following vaccination or adverse events, when patients have to stop efalizumab treatment. When treatment was stopped abruptly in controlled studies, relapse of psoriasis was reported, with exacerbation and new morphology of psoriasis (see Table 1 for definitions of terms such as 'relapse', 'rebound' and 'flare') [11]. There is currently little evidence-based medicine to guide management and treatment of patients after discontinuation of efalizumab. This study (protocol # IMP25180) evaluated five

regimens of standard systemic treatments for psoriasis that have been in use for a number of years, with a view to identifying appropriate therapy for the treatment of 'inflammatory recurrence' following discontinuation of efalizumab. The term 'inflammatory recurrence' was used in this study to cover two scenarios that may prompt reinitiation of treatment in routine clinical practice: (1) patients experience worsening of psoriasis soon after discontinuing treatment (within 2–3 months) that is not considered to reflect worsening due to the natural course of the disease, but that has not worsened sufficiently to constitute a rebound; or (2) patients have discontinued a psoriasis treatment due to an inflammatory disease flare but, following discontinuation, require treatment to prevent a rebound. For both these scenarios, it is important to re-initiate treatment promptly to prevent a rebound of psoriasis, which has been reported in approximately 5% of patients following cessation of efalizumab treatment[12] However, it should be noted that the second scenario is very uncommon – in phase III studies of efalizumab only 0.6% of efalizumab-treated patients discontinued treatment due to recurrence of psoriasis[13].

Table 1. Definitions of commonly-used terminology used by the US National Psoriasis Foundation (NPF), the European Medicines

Term	NPF [20]	EMEA [21]	This study
During treatment			
Flare	Typical or unusual worsening of disease during treatment and/or the occurrence of new psoriasis morphologies.	Not defined.	Not used
Following treatment discontinuation			
Recurrence	Not defined	The EMEA recommend the use of recurrence as an endpoint in long-term studies provided that it is clearly defined.	The term 'inflammatory recurrence' includes (a) patients with worsening of psoriasis within 2 months of discontinuation from efalizumab treatment to a level less severe than a rebound and (2) patients who have discontinued a psoriasis treatment due to an inflammatory disease flare but, following discontinuation, require treatment to prevent a rebound.
Relapse	Loss of 50% of PASI improvement from baseline in patients who achieve a clinically meaningful response (≥ 50% improvement in PASI score from baseline).	A reduction of >50% in PASI from the achieved maximal improvement in PASI score. Subjective alternatives: a relapse of psoriasis necessitating the re-initiation of treatment. A simple worsening of psoriasis beyond 2 months of therapy may represent the natural course of the disease (relapse) rather than a rebound associated with drug.	Not used
Rebound	A PASI of 125% of baseline or new generalized pustular, erythrodermic, or more inflammatory psoriasis occurring within 3 months of stopping therapy. Worsening occurring after 3 months of therapy may represent the natural course of the disease rather than a rebound associated with the drug.	Worsening of psoriasis over baseline value (e.g. PASI>125%) or new pustular, erythrodermic or more inflammatory psoriasis occurring within 2 months of stopping therapy. A 2-month boundary separating relapse and rebound is drawn on theoretical grounds and is more or less arbitrary.	Not used

This study was intended to mimic current practice and hence a naturalistic approach, in which the physician chose the most appropriate therapy, was pursued. The main objective was to provide guidance for appropriate management of inflammatory recurrence before its progression to rebound.

Methods

This was an open-label, investigational study carried out in nine centres on patients with moderate-to-severe plaque psoriasis. The study was carried out according to Good Clinical Practice guidelines and the Declaration of Helsinki; the protocol was approved by Research Review Board, Inc., and all patients provided signed informed consent. Patients were enrolled in the study if: (1) they had worsening of psoriasis within 2 months of discontinuation from efalizumab treatment in other studies, which in the

opinion of the investigator had not worsened sufficiently to constitute a rebound but that required re-initiation of treatment or, (2) had previously discontinued an efalizumab study due to an inflammatory disease flare. To cover both these scenarios, the term 'inflammatory recurrence' has been used. Patients were included if the recurrence was related to the disease previously treated with efalizumab and were excluded if the recurrence was considered to be part of the natural disease progression, which occurs more slowly (i.e. a relapse; see Table 1 for the EMEA definition of 'relapse').

Eligible patients received 12 weeks of systemic psoriasis therapy during the study as soon as inflammatory recurrence had been identified by the investigator. In order for the study to closely reflect routine clinical practice, attending physicians were free to judge which patients had worsening of disease that had not progressed to rebound and subsequently to choose the therapy they considered most appropriate for each individual patient from five predefined regimens. Physicians could switch among these therapies during the course of the study if it was deemed necessary. The standard approved psoriasis therapy regimens were:

• cyclosporin: initial dose 4.0–5.1 mg/kg/day until clinical improvement (as judged by the investigator), followed by a 50% reduction in dose every 2 weeks

• retinoids: initial dose 25–50 mg/day until clinical improvement (as judged by the investigator), followed by a 50% reduction in dose continuing for 8 weeks, at which time therapy was stopped

• corticosteroids: initial dose 0.25–0.5 mg/kg/day until clinical improvement (as judged by the investigator), followed by a 50% reduction in dose every 2 weeks

• methotrexate: initial dose 20–25 mg/week until clinical improvement (as judged by the investigator), followed by a 25% reduction in dose every 2 weeks

• combined therapy: systemic corticosteroids plus methotrexate, utilising both of the above regimens in combination.

The physician's global assessment (PGA) is a simple and quick-to-use assessment of clinical status in patients with psoriasis. The PGA is familiar to physicians and is the standard measure of disease severity in current clinical practice. Therefore, PGA of change was considered to be the simplest and most appropriate measure to assess treatment efficacy in the present study. GA of change was categorized according to seven ratings: 'clear' (100% improvement from baseline), 'excellent' (75–99%), 'good' (50–74%), 'fair' (25–49%), 'slight' (1–24%), 'unchanged' (no change in clinical signs and symptoms from baseline) and worse' (deterioration of clinical signs and symptoms from baseline). The disease was classified according to the morphology as inflammatory, plaque, papular/pustular, erythrodermic or inverse psoriasis and individual patients could have more than one type. The proportion of patients with each type was evaluated at the start and end of treatment.

This was a pilot investigation designed to collect information that would help plan future management strategies for patients who experience inflammatory recurrence after discontinuing efalizumab. There was no randomisation, all patients were analysed as treated and no formal statistical analysis was carried out. Owing to the need for treatment to control psoriasis, some patients were already allocated to one of the study drugs at the time of enrolment into the study. For these patients, baseline data were collected retrospectively, while data were collected prospectively for patients who were prescribed their initial psoriasis treatment at the time of enrolment. As the results were qualitatively similar for the two subgroups, the results are presented only for the two subgroups analysed together.

Results

A total of 41 patients were enrolled in the study (24 retrospectively and 17 prospectively), and their demographic details are summarised in Table 2 according to the systemic treatment initially prescribed by the attending physician. The age and gender profiles were similar across treatment groups. The systemic treatment most commonly prescribed was methotrexate, which was given as a single therapy to 20 patients; this was followed by cyclosporin, given to 10 patients, and corticosteroids, given to eight patients. For the majority of the patients in each treatment group, administration of one or more of the other systemic treatments was possible.

There were five patients in total who discontinued treatment before completing 12 weeks of the study. Three of these patients were from the methotrexate group: two discontinued due to patient decision and one was lost to follow- up; of the remaining two patients who discontinued prematurely, one discontinued from the cyclosporine group due to lack of efficacy, and one discontinued from the combined methotrexate plus corticosteroid group due to patient decision.

Assessment of PGA response

PGA for changes in disease was rated on a seven-point categorical scale from improvement resulting in clear of disease to worsening of disease. The proportions of patients categorised as 'good', 'excellent' or 'cleared' are shown in Table 3. The results in Table 3 are summarized according to the initial treatment prescribed to manage inflammatory recurrence (referred to as 'first treatment'), as well as according to the treatment that the patient was receiving at the end of the study (referred to as the 'last treatment'). This categorization of the results was designed to account for six patients who were switched between treatments during the study; similar results were observed when PGA was summarised by the first or last treatment. Cyclosporin provided the most favourable response, with a 'good', 'excellent'

or 'cleared' improvement recorded for 7/10 (70.0%) patients who started on the drug. A 'good', 'excellent' or 'cleared' rating was also recorded for 9/20 (45.0%) patients who started on treatment with methotrexate.

Changes in psoriasis morphology

Psoriasis morphology at the start and end of treatment is summarised in Table 4, according to the last treatment prescribed. As morphology of disease was not available for all patients, the data are shown as patients with a particular morphology as a proportion of the number of patients with available data at baseline. For all treatment groups combined, 21/27 (77.8%) patients with baseline morphology data had inflammatory psoriasis at entry. After treatment with a systemic psoriasis therapy, the prevalence of inflammatory disease was reduced to 19.2% of the patients. Methotrexate appeared to provide the best response for inflammatory psoriasis: the prevalence was reduced from 84.6% at baseline to just 8.3% at the end of treatment. Methotrexate also appeared to reduce the prevalence of papular/pustular psoriasis more than the other treatments.

The adverse event profile associated with each of the medications has been well documented, and the safety results were consistent with the known profiles. Across all treatment groups, 14 patients (34.1%) had at least one adverse event. Adverse events were considered to be possibly or probably related to treatment in eight patients (19.5%). During the study, there were no deaths, serious adverse events, or discontinuations due to adverse events.

Discussion

Efalizumab has been developed for long-term treatment of psoriasis, and clinical studies have shown increasing response with longer treatment duration. However, on discontinuation of treatment there have been reports of rebound of psoriasis symptoms, mainly in non-responding patients [11,14]. Rebound can occur with other psoriasis medications as was shown many years ago after stopping systemic corticosteroids [15]

as well as cyclosporin [16, 17]. If alternative therapies are instituted immediately when inflammatory recurrence is observed, development of rebound may be prevented. This analysis was a preliminary exploration of appropriate alternative therapeutic regimens for control of inflammatory disease recurrence in patients discontinuing efalizumab, such that progression to rebound can be avoided. As an exploratory study, there are a number of inherent limitations that should be accounted for when interpreting the results,

Table 2. Patient demographics at baseline, according to systemic therapy prescribed as first treatment.

	Methotrexate (N = 20)	Cyclosporin (N = 10)	Corticosteroids (N = 8)	Combined[a] (N = 2)	Retinoids (N = 1)	All patients (N = 41)
Age (years)						
Mean ± SD	49 ± 10	43 ± 12	44 ± 11	47 ± 3	41	46 ± 11
Range	28–67	20–58	20–60	45–49	-	20–67
Gender (n (%))						
Male	13 (65.0)	5 (50.0)	5 (62.5)	1 (50.0)	1 (100)	25 (61.0)
Female	7 (35.0)	5 (50.0)	3 (37.5)	1 (50.0)	0	16 (39.0)
Ethnicity (n (%))						
Caucasian	15 (75.0)	10 (100)	8 (100)	2 (100)	1 (100)	36 (87.8)
Asian	2 (10.0)	0	0	0	0	2 (4.9)
Other	3 (15.0)	0	0	0	0	3 (7.3)

Table 3: Patients with a PGA change[a] of 'good', 'excellent' or 'cleared', according to first treatment (assigned at baseline) and last

	Methotrexate	Cyclosporin	Corticosteroids	Combined[b]	Retinoids	All patients
First treatment (n (%))	9/20 (45.0)	7/10 (70.0)	2/8 (25.0)	0/2 (0.0)	0/1 (0.0)	18/41 (43.9)
Last treatment (n (%))	9/18 (50.0)	9/12 (75.0)	4/8 (50.0)	1/2 (50.0)	0/1 (0.0)	23/41 (56.1)

* At the investigators' discretion, six patients were switched between treatments during the study.
[a]Change from baseline.
[b]Combined systemic corticosteroids plus methotrexate.
PGA, physician's global assessment.

Table 4. Disease morphology at start of treatment (baseline) and at Week 12 or withdrawal (endpoint), by last treatment prescribeda.

]including the small number of patients included in each of the treatment groups. It should also be noted that, due to the need for treatment to control psoriasis, some patients were already allocated to one of the study drugs at the time of enrolment into the study. Therefore, baseline data were collected retrospectively for these patients. In clinical trials, the Psoriasis Area and Severity Index (PASI) is the most commonly used measure of disease severity, but in a clinical setting it is difficult to use due to its complexity. The PGA, which is more simple and quick to use compared with the PASI is, therefore, the more commonly used assessment in current clinical practice. In a placebo-controlled clinical study of efalizumab for the treatment of patients with moderate-to-severe plaque psoriasis, close agreement was found between the PASI and PGA when both were used to measure improvement in psoriasis [18]. In addition, a double-blind trial directly compared ratings with the PASI, PGA and a National Psoriasis Foundation scoring system and found a strong concordance between them [19]. Therefore, PGA was considered to be the simplest and most appropriate measure for use in the present study. The results from the present analysis indicated that methotrexate and cyclosporin were effective in alleviating the symptoms of recurrence of psoriasis. Systemic corticosteroids and retinoids appeared less effective in treating inflammatory recurrence, but the small number of patients means that further studies with these therapies are still necessary.

Conclusion

The results from this study indicate that inflammatory recurrence after discontinuation of efalizumab therapy is a manageable event. In order to prevent progression to established rebound, a number of therapies and approaches are available to physicians, including short courses of cyclosporin or methotrexate. Further largerscale studies are required to confirm the present results.

Competing interests

KAP, DT and LR have received consultancy honoraria from Serono.

Authors' contributions

KAP, DT and LR all contributed to the design and conduct of the study, and to the analysis and interpretation of the

results. All authors read and approved the final manuscript.

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ASSOCIATION OF TOLL-INTERACTING PROTEIN GENE POLYMORPHISMS WITH ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a common inflammatory skin disorder, affecting up to 15% of children in industrialized countries. Toll-interacting protein (TOLLIP) is an inhibitory adaptor protein within the toll-like receptor (TLR) pathway, a part of the innate immune system that recognizes structurally conserved molecular patterns of microbial pathogens, leading to an inflammatory immune response.

Background

Atopic dermatitis (AD) is an inflammatory skin disease infancy and affects up to 16% of children [1]. AD has a characterized by pruritus and chronic or relapsing ecze-multifactorial background, with genetic predisposition and environmental factors contributing to disease susceptibility [2]. In industrialized countries AD prevalence has increased during the past decades [3], and it has been postulated in the so-called 'hygiene hypothesis' that the lack of contact to microbial products in early infancy might at least in part be responsible for this increase [4]. There is evidence from prospective studies to support an inverse relationship between AD and exposure to endotoxin, a cell membrane component of gram negative bacteria, early day-care attendance and animal exposure [5].

Recognition of microbial products such as endotoxin is mediated by the innate immune system. Toll-like receptors (TLRs) are a family of evolutionarily conserved receptors that recognize pathogen-associated molecular patterns (PAMPs), leading to an inflammatory response by induction of interleukins and other pro-inflammatory proteins [6]. Polymorphisms in TLR genes have been implicated in various diseases [7] including AD [8]. Yet, the effect of genetic variation in TLR downstream signalling pathways has not been sufficiently studied yet. Tollinteracting protein (TOLLIP) is an adaptor protein that acts as an inhibitory factor in the TLR-signalling cascade [9-11]. It functions downstream of MyD88 and TIR domain containing adaptor protein (TIRAP) through inhibition of Interleukin-1 receptor associated kinase 1 (IRAK1) [10] and controls the magnitude of inflammatory cytokine production in response to endotoxin [12]. The TOLLIP gene is located on chromosome 11p15 and comprises 6 exons encoding a 274 amino acid transcript. The 11p15 region has so far not been reported as a linkage region for AD in the four published genome screens [13]. Yet, association studies are generally supposed to have a greater power to detect common alleles with modest

effects on disease susceptibility than linkage studies [14]. Furthermore, dysregulated inhibition in the TLR-signalling cascade may cause a pathologically increased or reduced inflammatory response, and variations in the ST2 gene, encoding another inhibitory protein in the TLR pathway, were recently found to be associated with AD [25]. Therefore, we considered the TOLLIP gene an interesting candidate gene for AD.

We screened the entire coding region of the TOLLIP gene by single strand conformation polymorphism (SSCP) analysis in 50 AD patients in order to identify coding variation that might play a role for AD pathogenesis. Subsequently, the identified polymorphisms were genotyped in 317 AD patients and 224 healthy controls to evaluate a possible association with AD. In order to provide a more complete and valuable assessment of variation in the TOLLIP gene, we additionally typed four non coding polymorphisms (located in the promoter and intronic regions as well as in the 3'UTR) that were chosen from the HapMap

Methods
Subjects

317 unrelated patients with atopic dermatitis were recruited by a consultant specialist for AD (Q.P., Gladbeck, Germany), including 193 children and 124 adults. The AD diagnosis was based on the presence of clinical features, including pruritus, eczema with age-dependent differences in location, xerosis and chronic or relapsing dermatitis. In addition, all investigated AD patients had a positive family history for atopic diseases. 224 control samples from adults without known allergies, asthma or AD were collected in the same private practice as the AD patients. We specifically chose to use non-allergic adults as controls because for diseases as frequent as AD, the risk remains very high for asymptomatic children to develop an allergic disease during childhood or even adulthood [16,17]. The control subjects underwent clinical examination in order to exclude symptoms of AD, asthma or allergic rhinitis, had no self-reported allergies or allergic symptoms and no first degree relatives with known allergic diseases. All patient and control subjects were Caucasians of German origin. Informed consent was obtained from all subjects. The study was approved by the Ethics Committee of the Ruhr-University, and the Declaration of Helsinki protocols were followed.

Preparation of DNA and RNA

DNA was extracted from EDTA anti-coagulated peripheral blood by using a standard salting-out method [18]. Total RNA samples were extracted from EBV-transformed lymphoblastoid cell lines using TriFast reagent (Peqlab) according to the manufacturer's instructions up to the point of phase separation. Afterwards, the aqueous phase was transferred to an RNeasy column (Qiagen, Hilden, Germany) and processed according to the manufacturer's protocol. OD260 and OD280 were determined and the RNA was stored at -70°C until use.

Single strand conformation polymorphism analysis

The entire coding region of the TOLLIP gene was screened for polymorphisms by polymerase chain reaction (PCR) with consecutive single strand conformation polymorphism (SSCP) analysis. PCR reactions were performed in a total volume of 10 .l, containing 50 ng DNA, 200 mmol of each dNTP, 0.4 U Taq polymerase (Genecraft, Munster, Germany), GC-Buffer (Genecraft, Munster, Germany), and 0.1 .l [32P] .-CTP (10 mCi/ml). Thermal cycling was conducted in a thermal cycler (Biometra, Gottingen, Germany). After a denaturation step at 95°C for 5 minutes followed by two initial cycles at 6°C and 3°C above the annealing temperature, 28 cycles with 95°C (30 sec), annealing temperature (30 sec) and 72°C (30 sec) were run. Further details for primers and conditions are given in table 1. For SSCP analysis, 3 .l of the PCR product was mixed with 7 .l of SSCP loading buffer (95% formamide, 20 mM EDTA, 0.05%

xylene cyanol and 0.05% bromophenol blue), denatured for 5 minutes at 95°C and thereafter directly cooled on ice. Then 2.5 .l were applied on 6% polyacrylamide gels (38% acrylamide, 2% bisacrylamide) containing 1. TBE buffer (890 mM Tris-borate, 20 mM EDTA, pH 8.3) and 10% glycerine in a SQ3 apparatus (Hoefer, Freiburg, Germany) at 55 W for about 210 minutes. The room temperature was constantly held at 4°C during SSCP analyses.

DNA sequencing

DNA samples showing mobility shifts on SSCP gels were directly sequenced on an automated capillary DNA sequencer (MegaBace 1000, Amersham Biosciences), using the BigDye cycle sequencing kit (Applied Biosystems, Darmstadt, Germany) as described in the manufacturer's instructions.

Genotyping

All six polymorphisms in the TOLLIP gene were genotyped by restriction enzyme digestion (see Table 1). Patient and control samples were amplified using the same primers and conditions as described above, except for the inclusion of radioactivity. After digestion with the respective enzymes for at least three hours, the fragments were separated on 2% agarose gels in 1. TBE buffer (45 min, 200 V) and visualized by staining with ethidium bromide.

Measurement of mRNA levels by quantitative real-time PCR

We carried out real-time PCR on an I-Cycler (Bio Rad Laboratories, Hercules, USA). The quantity of PCR products was determined after each round of amplification using the fluorescent dye SYBR Green I (Qiagen), which binds double-stranded DNA.

The primer sequences (F: 5'AGTACGGAGGCGCAGTGG-3'; R: 5'-AGGCGCAGTCGGCAGTAG-3') represent parts of two adjacent exons in order to prevent amplification of potential traces of contaminating genomic DNA. PCR reactions were run in triplicates (95°C for 5 min, 56°C for 30 sec, 95°C for 1 min, 55°C for 30 sec). Fluorescence was recorded at the end of each extension step, and a melting curve was obtained at the end of each run. Quantification of the house-keeping gene glyceraldehyde-3-phosphate dehydrogenase(GAPDH-) mRNA (primers F: 5'-TGTGTCCGTCGTGGATCTGA-3'; R: 5'-CCTGCTTCACCACCTTCTTGA-3'; product size 76 bp) was used as a control for data normalization. After the PCR, products were analyzed on agarose gels in order to verify band sizes and purity. Expression was assessed by evaluating threshold cycle (CT) values. The CT values were calculated by the system software (iCycler), and the relative amount of expressed RNA was calculated using Livak 's method [19].

Statistics

Allele and genotype frequencies were compared between the groups of patients and healthy individuals using a .2 test. Additionally, we used logistic regression to test for significant associations between AD status and single SNPs alone as well as additional pairwise interactions between SNPs in the TOLLIP gene. Significance was assessed by a Wald test on significant deviations of the regression parameters from 0. Correction for multiple testing of SNPs that are in LD with each other was applied according to the method introduced by Li & Ji [20] which improves an approach proposed

Table 1. Primer sequences, PCR conditions and restriction enzymes used for mutation analysis and genotyping of selected polymorphisms in the TOLLIP gene.

Amplicon	Rs number	Amino acid	Primer	Annealing temperature	$MgCl_2$ (mmol/l)	Restriction enzyme
TOLLIP-526 C/G	5743854	-	F: GGGTGACCTTCGGACGTG R: CATCTTTAGCCCTGTGAAACAG	57°C	2	Hin6I
TOLLIP exon 1*	-	-	F: GACAACTGTCTCCGTCGCA R: TGGGTCAGGGCTACTGCT	55°C	2	-
TOLLIP intron1a	5743867	-	F: ACTCTCCCAGCACCTGACGCTTAAG R: ACCAGCGCTACCAACTGTGGCGAT	61°C	4	MboI
TOLLIP intron1 b	11042484	-	F: GACCCAGCCGTCTGCAGGG R: TCCATGGCACAGGCAGGTACG	62°C	2	Hin6I
TOLLIP exon 2†	-	-	F: ACCCTGACTCACTGGCCTC R: TTTCAACATCACACACGTTTCA	58°C	2	-
TOLLIP exon 3*	-	-	F: GTTGGCACCTCCTTTTCCTGAC R: CAGGTGTGTCCCCACGGC	66°C	2	-
TOLLIP exon 4	3750920	Pro139Pro	F: GGGCCTCTCCCTCTTGTC R: TCAGAACGTGAGCCCTGC	60°C	3	MspI
TOLLIP exon 5†	-	-	F: GGTTCTGATGGGTGCATGTTCC R: ACCTGCCCTAGGCCCTGG	66°C	2	-
TOLLIP exon 6	5744015	Ala222Ser	F: TTCCGACGTTTTTACCAAACTTGAT R: GCGTGTCCAAAGAGCGGG	63°C	2	MwoI
TOLLIP 3'UTR	3750919	-	F: AGCCTGACTCTCACACTCAGCA R: GGGAGCAAAACCTTGATACCAA	58°C	3	Alw26I

F = forward primer, R = reverse primer,
*Amplicons were only amplified for SSCP analysis; no coding variation was discovered with this method

by Nyholt [21], and consequently single-test p-values < 0.0102 were considered to be significant. Deviations from Hardy-Weinberg equilibrium were evaluated using the FINETTI program. The FamHap software [22] was used for haplotype frequency estimation. 95% confidence intervals for the haplotype frequency estimates were constructed using 10,000 bootstrap samples with replacement (non-parametric bootstrap). We performed power analyses with the Genetic Power Calculator program [23]. Potential binding sites for transcription factors at the -526 C/G locus were evaluated using a transcription factor prediction program [24]. For quantitative real-time PCR, the relative amount of expressed RNA was calculated by using Livak's method [19]. Differences between genotypes were assessed by using the REST 2005 beta V1.9.9 software [25].

Results

Screening of the coding region of the TOLLIP gene revealed two exonic polymorphisms: a synonymous variation in exon 4 (Pro139Pro) and an amino acid substitution in exon 6 (Ala222Ser). Four additional SNPs in noncoding regions (-526 C/G, Intron1a, Intron1b, 3'UTR) were chosen from the HapMap database [15]. Evaluation of these polymorphisms in 317 AD patients and 224 controls showed a modest association of the -526 C/G promoter SNP with AD (table 2). The C allele of the -526G/C promoter polymorphism was significantly more frequent in AD patients than in healthy controls (12.7% vs. 7.7%, uncorrected p-value = 0.012). This polymorphism was in strong linkage disequilibrium (LD) with the Intron1a SNP, and the Pro139Pro variation was in moderate LD with the 3'UTR SNP ($r2 = 0.64$ and 0.20, resp.). Therefore, we felt that Bonferroni correction for independent tests would be overly conservative and applied Li & Ji's multiplicity correction for SNPs that are in LD with each other and, thus, dependent [20]. This approach yielded a significance level of 0.0102 to keep an overall level of 0.05 in both the cases and the control group.

Our finding (p = 0.012), therefore, showed borderline significance, being slightly higher than the significance level. Additionally, the Intron1a G allele was more frequent in AD patients (8.8% vs. 5.6%) while the 222Ser allele showed an increased frequency in healthy controls (5.4% vs. 2.7%). Yet, significance was not evident after correction for multiple testing for both polymorphisms. For the other three variations, no difference in allele or genotype frequencies was found between AD patients and controls. We repeated our analyses within the subgroup of patients with elevated IgE levels and saw the same trend within this subgroup, with the -526G, the Intron1a G allele and the 222Ala allele being more prevalent in cases than in controls (data not shown). Yet, because of the reduction in sample size, the results did not reach statistical significance. All investigated polymorphisms were in Hardy-Weinberg equilibrium in cases and controls. We performed power analyses with the Genetic Power Calculator [23]. Given a multiplicative model with a genotypic relative risk of 2 for heterozygotes and 4 for homozygotes and a D' of 0.9, we would have 96% power to detect a potential effect. Choosing more conservative parameters, with a genotypic relative risk of 1.5/2.25 and D' of 0.8, would yield only 48% power. Haplotype analysis did not yield significant results (table 3). We did not find evidence for a pair wise interaction between SNPs within the TOLLIP gene (data not shown).

Because of the observed borderline association of the -526 C/G polymorphism with AD, we searched for potential binding sites for transcription factors at this locus using a transcription factor prediction program [24]. Differential binding of two transcription factors was predicted for the two different alleles at this locus. While the G allele gave a putative binding site for the AP2-. transcription factor, the C allele showed a putative binding site for E2F. The mRNA expression in B-lymphocyte cultures from six probands with the C/C genotype and six probands with the G/G genotype did not show any differences in expression between the genotypes (figure 1).

Discussion

The innate immune response initiated by TLRs is an important mechanism in defense against pathogenic microorganisms, and variations in TLR genes have been implicated in the pathogenesis of allergic as well as autoimmune diseases [7]. Several studies have pointed out that the innate immune system plays an important role in AD pathogenesis. For example, epidemiological studies showed an inverse relationship between AD and exposure to endotoxin (lipopolysaccharide, LPS), early day-care attendance and animal exposure [5], suggesting that lack of contact to microbial products might increase risk for AD. Further, TLRs were found to be up-regulated in circulating monocytes from AD patients [26]. A polymorphism in the TLR2 gene was associated with a severe AD phenotype [8]. Additionally, variations in the CD14 gene, encoding part of the cell membrane receptor for LPS, as well as in the CARD15 gene, encoding an intracellular LPS receptor, have shown associations with AD [27,28]. Thus, genes in the downstream pathway of TLR signalling also constitute reasonable candidate genes for this frequent skin disease. We demonstrate here first evidence for an association of AD with variation in the TOLLIP gene, encoding a protein with an inhibitory function in the TLR signalling pathway.

Screening of the coding region of the TOLLIP gene by SSCP identified two coding variations: Pro139Pro and Ala222Ser. The rate of detection of nucleotide variants by SSCP varies between 80% and close to 100% under optimized conditions [29].

Table 2. Genotype and allele frequencies of TOLLIP polymorphisms in AD patients and healthy controls*.

Polymorphism	Genotype	Allele	AD	Controls	p-value
-526 C/G	C/C		240 (76.9%)	181 (84.6%)	
	C/G		65 (20.8%)	33 (15.4%)	
	G/G		7 (2.2%)	0 (0%)	
	n		312	214	0.08
		C	545 (87.3%)	395 (92.3%)	
		G	79 (12.7%)	33 (7.7%)	
		n	624	428	0.012
Intron1a	A/A		265 (83.6 %)	199 (88.8%)	
	A/G		48 (15.1%)	25 (11.2%)	
	G/G		4 (1.3%)	0 (0%)	
	n		317	224	0.16
		A	578 (91.2%)	423 (94.4%)	
		G	56 (8.8%)	25 (5.6%)	
		n	634	448	0.045
Intron1b	A/A		2 (0.6%)	3 (1.3%)	
	A/G		54 (17.3%)	39 (17.5%)	
	G/G		256 (82.1%)	181 (81.2%)	
	n		312	223	0.903
		A	58 (9.3%)	45 (10%)	
		G	566 (90.7%)	401 (90%)	
		n	624	446	0.66
Pro139Pro	C/C		92 (30.4%)	64 (30.0%)	
	C/T		147 (48.5%)	113 (53.1%)	
	T/T		64 (21.1%)	36 (16.9%)	
	n		303	213	0.43
		C	331 (54.6%)	241 (56.6%)	
		T	275 (45.4%)	185 (43.4%)	
		n	606	426	0.52
Ala222Ser	Ala/Ala		293 (94.5%)	198 (89.6%)	
	Ala/Ser		17 (5.5%)	22 (9.6%)	
	Ser/Ser		0 (0%)	1 (0.5%)	
	n		310	221	0.049
		Ab	603 (97.3%)	418 (94.6%)	
		Ser	17 (2.7%)	24 (5.4%)	
		n	620	442	0.02
3'UTR	G/G		193 (61.5%)	133 (60.5%)	
	A/G		105 (33.4%)	76 (34.6%)	
	A/A		16 (5.1%)	11 (5.0%)	
	n		314	220	0.965
		G	491 (78.2%)	342 (77.7%)	
		A	137 (21.8%)	98 (22.3%)	
		n	628	440	0.86

*According to the method of multiplicity correction for SNPs in LD that was introduced by Li & Ji [20], we considered p-values < 0.0102 as significant.

Thus, it is possible that rare varia-tions might have been missed with this approach. Yet, for polymorphism (-526 C/G) We found a modest association of a promoter database.

in the TOLLIP gene with AD, multifactorial diseases like AD, common instead of rare Since Bonferroni correction has been controversial for variations have been

suggested to play a role for patho-genetic association studies because it might be overly congenesis [30]. Therefore, we chose to additionally type four servative [31], we chose to use a method for multiplicity frequent SNPs in non-coding regions from the HapMap correction when SNPs in linkage disequilibrium (LD) are

Table 3. TOLLIP haplotype frequencies in AD patients and controls.

Haplotype	Frequency in AD patients (n = 312)	95%-CI*	Frequency in controls (n = 222)	95%-CI*
C-A-G-T-G-G	0.437	0.396 0.477	0.421	0.376 0.466
C-A-G-C-G-A	0.202	0.169–0.236	0.205	0.169–0.245
C-A-G-C-G-G	0.106	0.081–0.133	0.138	0.104–0.175
C-A-A-C-G-G	0.091	0.069–0.114	0.090	0.063–0.119
G-G-G-C-G-G	0.083	0.061 0.107	0.055	0.034 0.076
G-A-G-C-G-G	0.031	0.016–0.046	0.023	0.009–0.039
C-A-G-C-T-G	0.026	0.014 0.039	0.041	0.022 0.061

*95% confidence interval for the haplotype frequency estimate using 10,000 bootstrap samples with replacement (non-parametric bootstrap).

tested that was introduced by Li & Ji [20]. Our observed pvalue of 0.012 for the -526 C/G promoter SNP was borderline significant with respect to Li & Ji's method (0.0102). We therefore believe that it might represent a true association. Haplotype analysis did not yield additional information. Interestingly, functional SNPs in the distal promoter of the *ST2* gene were recently found to be associated with AD in the Japanese population [32]. Both TOLLIP and ST2 exert inhibitory functions in the TLR cascade [9,33], and for the *TOLLIP* gene we also saw the most significant although borderline association with the promoter SNP. Therefore, we decided to further explore the role of the - 526 C/G variation for AD. Investigation of potential binding sites for transcription factors at the -526 C/G locus using a transcription factor prediction program predicted differential binding of two transcription factors (AP2-γ and E2F) for the two different alleles at this locus. Interestingly, E2F is an important factor in the control of skin pro iferation [34],
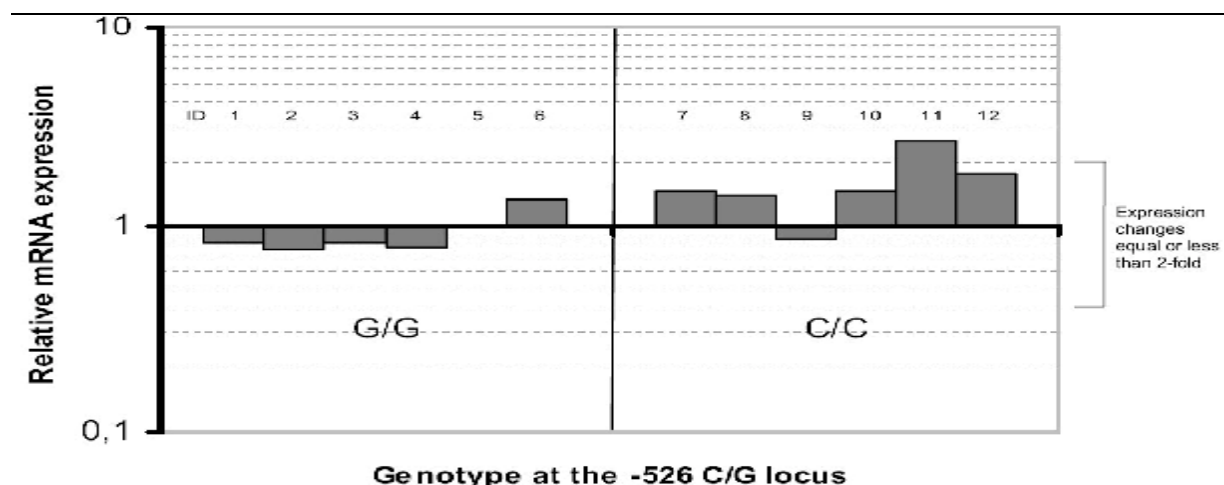
Figure 1
TOLLIP mRNA expression in six individuals with the genotype GG (ID numbers 1–6) and six individuals with the genotype CC (ID numbers 7–12) at the -526 C/G locus. Total RNA samples were extracted from EBV-transformed lymphoblastoid cell lines and mRNA levels measured by quantitative real-time PCR. For each individual, mRNA expression is shown relative to the mean expression of the six individuals with the opposite genotype. The range of expression changes is less than 2-fold for each individual except ID11. No significant differences in *TOLLIP* mRNA expression between genotypes were obvious.

and the AP2 family appears to regulate the expression of genes required for the development of ectodermal tissues, including skin [35]. In order to detect a possible direct influence of the TOLLIP -526C/G polymorphism on mRNA expression, we performed quantitative real-time PCR for measurement of mRNA amounts in lymphoid cell cultures from six probands with the C/C and six with the G/G genotype at this locus. Yet, we were unable to find differences in mRNA expression with this method. There are several explanations for this finding. First, a variation that is more distal to the promoter and in LD with the -526 C/G polymorphism or some promoter haplotypes might be the true disease-associated variation. In fact, the recently identified functional SNPs in the ST2 promoter are also located very distal from the transcription start (-26999 and -27639, resp. [32]). Second, measuring mRNA expression via quantitative real-time PCR may not represent the most sensitive method to detect moderate differences in promoter function. Third, expression studies in keratinocytes instead of blood B-lymphocytes would be more informative for a chronic skin disease such AD. Finally, since our association results are somewhat borderline, there may indeed be no functional significance of the analyzed promoter SNP. Yet, functional studies including electro-mobility shift assays (EMSA) are needed to further evaluate the functional relevance of the -526 C/G promoter polymorphism in the TOLLIP gene.

We cannot exclude the possibility that the association result we found for the TOLLIP promoter polymorphism may be caused by another SNP in TOLLIP or a neighbouring gene that is in LD with this variation. For example, the intron 1a SNP that is in LD with the -526C/T polymorphism and the Ala222Ser variation in exon 6 also showed marginal evidence for an association with AD. Further, we are aware of the fact that genetic association studies bear the risk of false-positive results caused by hidden population substructures. Yet, all our patients and controls were of German origin and recruited in North Rhine Westfalia. Even if some of the patient families and controls might originate from neighbouring European countries, a recent study demonstrated that linkage disequilibrium patterns are conserved across European samples for most gene regions [36]. Thus, we consider the risk that our results are caused by hidden population substructures to be marginal, at most. Yet, population stratification could in principle contribute to the borderline significant results we observed in our association study. Finally, the relatively small size of our sample bears the risk of small power, potentially causing false-negative association results. Yet, power analyses indicated that considering a multiplicative model with a genotypic relative risk of 2 for heterozygotes and 4 for homozygotes and a D' of 0.9, we would have a 96% power to detect a potential effect of a chosen marker.

Choosing more conservative parameters, with a genotypic relative risk of 1.5/2.25 and D' of 0.8, would yield only 48% power. On the other hand, the cohort we present here has been thoroughly recruited by a single physician, so that it constitutes a highly controlled sample with exclusion of many potential confounders. In any case, the borderline evidence for association of TOLLIP variation with AD that we present in this study clearly needs to be replicated in additional studies and populations in order to rule out false positive results.

Conclusion

We present first evidence for an association of TOLLIP variation with atopic dermatitis. Our results, although borderline, support the concept that genetic variation in the TLR system may play an important role in the pathogenesis of AD. In combination with recently published association findings for the ST2 gene [32], we suggest that dysregulation of inhibition in the TLR pathway might be of special importance. Yet,

the exact mechanism by which variation in negative regulators of TLR signalling may influence AD pathogenesis still needs to be explored. Targeting TLRs has already been discussed as a novel therapeutic option for allergic diseases [37,38]. Thus, better understanding of the molecular pathogenesis of AD could eventually lead to new options in prevention and treatment of this frequent skin disease.

List of abbreviations used

AD atopic dermatitis

LD linkage disequilibrium

PAMP pathogen-associated molecular pattern

PCR polymerase chain reaction

SNP single nucleotid polymorphism

SSCP single strand conformation polymorphism

TLR Toll-like receptor

TOLLIP Toll-interacting protein

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

TS performed the experiments and drafted the manuscript. QP and EPP recruited the patients as well as controls and collected clinical data. MN performed the statistical analyses. JTE participated in the design and coordination of the study. SH was in charge of the design and coordination of the study as well as the statistical analyses and finalised the manuscript. All authors read and approved the final manuscript.

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REPRODUCTIVE PERFORMANCE OF NORWEGIAN CATTLE FROM 1985 TO 2005: TRENDS AND SEASONALITY

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Declining reproductive performance is a serious breeding concern in many countries. To reveal the situation in Norwegian cattle, trends in reproductive performance were studied using insemination reports from 1985 to 2005 and data based on herd recording files from 1989 to 2005. The total number of first services was 469.765 in 1985 declining to 335.712 in 2005. The number of recorded herds and animals declined from 21.588 to 14.718 and 360.289 to 309.452 from 1989 to 2005, respectively. Sixty days non-return rate after single inseminations (NR60) increased from 68.1 in 1985 to 72.7% in 2005 ($p < 0.001$) and the number of services per inseminated animal (NIA) decreased from 1.8 to 1.6 ($p < 0.001$) from 1985 to 2005. However, return rates 0–3 days post insemination (RR0-3) increased from 6 to 12% in the same period ($p < 0.001$). NR60 was higher and the RR0-3 was lower in the summer season compared to the winter season during the whole period. A fertility index (FS), has been calculated from the herd recording files each year from 1989 to 2005. The average FS-index did not show a significant trend and the calving interval was also fairly constant between 12.4 and 12.6 months during this period. The average interval from calving to first and last insemination, respectively, increased from a low of 79 and 102 days in 1990 to a high of 86 and 108 days in 2005. Both intervals were consistently longer for cows in first lactation than for cows in later lactations. The percentage of inseminated animals reported culled because of poor fertility decreased from 6.0% in 1989 to 4.6% in 1996 and thereafter again increased to 6% in 2005. In conclusion, most fertility measures, mainly comprising the Norwegian Red (NRF) breed, show a relatively high level of reproductive performance with a positive or a relatively constant trend during the last two decades.

Background

In many countries there has been a decline in reproductive performance in dairy cattle. Several studies show increasing number of days from calving to first service and decreasing pregnancy rates, e.g. [1-5]. As a result, the number of inseminations per inseminated cow, days from calving to conception and calving intervals have increased. To improve fertility and save labour, various pharmaceuticals to control the oestrous cycle and to treat reproductive disorders are extensively used in many herds, e.g. [6,7]. During the last decades the productivity of dairy cattle has increased considerably in many countries, not least because of progress due to genetic improvement. However, a serious breeding concern is that estimates from a number of studies present unfavourable genetic correlations, on average near 0.3, between various fertility measures and production [8]. In contrast to many other countries, Norway has a long tradition of including fertility in the Total Merit Index (TMI). Viewed against this background, the primary objective of the present study was to describe the trends in some reproductive measures in Norway the last two decades. Seasonal variations in reproductive performance are also revealed.

Methods

The results obtained in the present study are based on insemination reports and herd recording files in Norway comprising 66.8% of the herds in 1985 increasing to 94.2% in 2005 [9]. AI-technicians and veterinarians report all inseminations into the AI-database, and they are only paid when the

inseminations are registered. From 1985 to 2005, the part of inseminations performed by veterinarians has increased from 45.8% to 59.7%. The rest of the inseminations was performed by technicians, but from 2002 also a small part by herdsmen, increasing from 0.3% to 0.7% in 2005. After attending an AI-course the herdsmen have to sign an agreement to report inseminations to the AI-database. Sixty days non return rates after single inseminations (NR60), return rates 0–3 days post insemination (RR0-3), average number of inseminations per animal inseminated (NIA) and seasonality are based on all inseminations performed in the country during the period, irrespective of membership in the milk recording system. Thus, these data are based on 469.765 number of first services in 1985 [10] declining to 335.712 services in 2005 [11].

Trends concerning age of heifers at first insemination, average number of days from calving to first (CFI) and last insemination (CLI), respectively, number of animals inseminated (I), calving interval and animals culled because of failure to breed (AC) were obtained from herd recording files from 1989 to 2005. During this period there was a decline in number of recorded herds from 21.588 to 14.718 and animals from 360.289 to 309.452. A fertility index, Fertility status (FS), was also calculated for each herd from the herd recording files every year from 1989 to 2005. FS index is expressed by the formula:

$$\frac{\left(\dfrac{NR60+RR0\text{-}3}{NIA}-\left(125\text{-}CLI\right)\right)\left(I\text{-}AC\right)}{I}$$

Comparisons of NR60, RR0-3 and NIA between years or groups were performed using chi-square analysis.

Results

The number of first inseminations every 5th year from 1985 to 2005 is shown in figure 1. The major part of the inseminations is performed with semen from the Norwegian Red (NRF) breed, varying from a high of 97.8% in 1985 to a low of 92.3% in 2003. Semen from other breeds are various beef breeds (4.2% in 2005), mainly used on NRF cattle, and other dairy breeds (3.0% in 2005) [11]. During the period of study, October – January represented the main breeding season with peaks in November and December. From February to September the monthly number of 1st services remained similar (Figure 2). The age of heifers at 1st insemination was at a low of 15.6 months in 1991 and increased to 16.2 months from 2001 to 2005. The average CFI interval has increased from a low of 79 days in 1990 to a high of 86 days in 2005 (Figure 3). The CFI interval for cows in first lactation was consistently longer than for cows in later lactations, increasing from 81 to 88 days and 78 to 84 days respectively, from 1990 to 2005. The average CLI interval has also increased during the period from a low of 102 days in 1990 to a high of 108 days in 2005 (Figure 4). The CLI interval for first lactation cows was also consistently longer than for cows in the second and later lactations, increasing from 106 to 113 days and 99 to 104 days respectively.

Figure 5 shows the trends concerning NR60 and RR0-3. The average NR60 has increased significantly from 68.1% in 1985 to 73.4% in 2002 ($p < 0.001$) and then declined to 72.7% in 2005. RR0-3 has increased from 6% in 1985 to 12% in 2005 ($p < 0.001$). The seasonal variation in NR60 every 5th year from 1985 to 2005 is shown in Figure 6. NR60 is consistently higher in the summer than in the winter. However, the difference between the highest summer month and the lowest winter month has decreased substantially from 10.4% in 1985 to 5.7% in 2005. Figure 7 shows the seasonal variation in RR0-3 every 5 year from 1985 to year 2005. RR0-3 is consistently higher during the winter months as compared to the summer months.
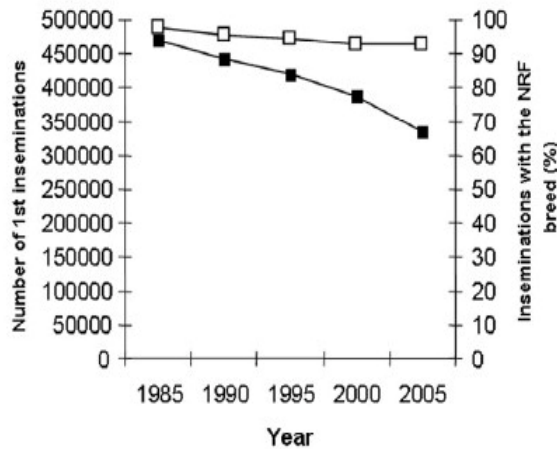
Figure 1
Total number of first inseminations (■) and percentages of inseminations performed with semen from bulls of the NRF breed (□) every 5th year from 1985 to 2005.
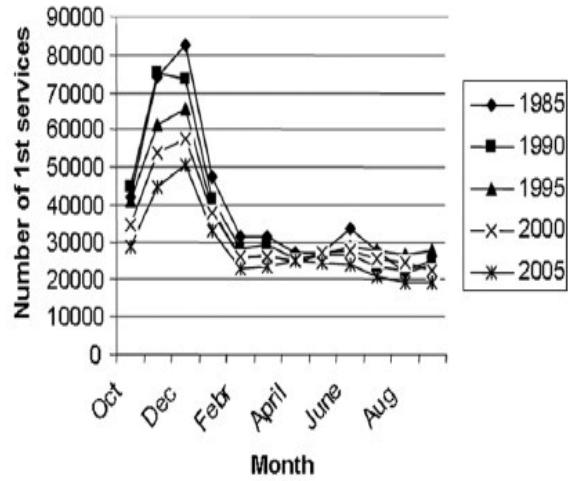
Figure 2
Seasonal distribution of first inseminations every 5th year from 1985 to 2005.

In 2005 RR0-3 reached a high of 15.2% in December and declined to a low of 7% in July. The overall average NIA has declined from 1.8 in 1985 to 1.6 in 2005. NIA for heifers (n = 96849), cows in 1st lactation (n = 85351) and cows with >1 lactation (n = 127252) were 1.5, 1.8 and 1.7 (P < 0,001) respectively for controlled animals in 2005. Data from 1989 to 2005 show each year similar differences in NIA between heifers, cows in 1st and >1 lactation. Figure 8 shows the average FS-index and calving interval for controlled animals from 1989 to 2005. The FS-index varying between 59.3 (1989) and 63.3 (1998), does not show a specific trend. Average calving interval in controlled animals has varied between 12.4 and 12.6 months during the same period also without showing a specific trend.
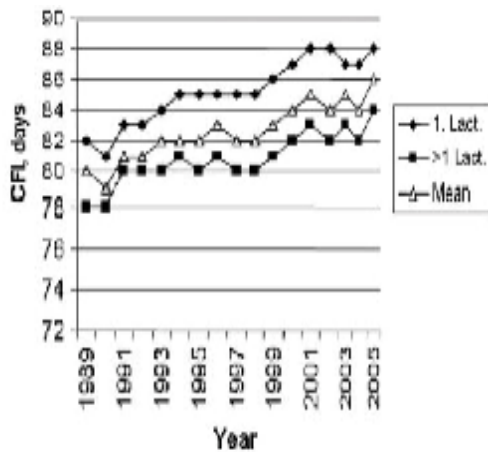
Figure 3
Average interval from calving to first insemination (CFI) in first lactation (♦), later lactations (■) and for all cows (△).
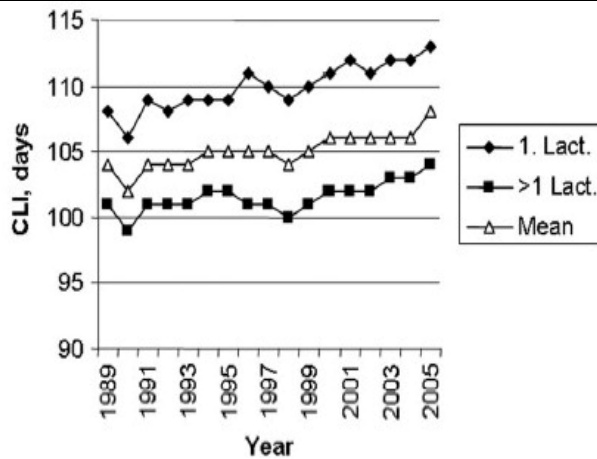
Figure 4
Average interval from calving to last insemination (CLI) in first lactation (♦), later lactations (■) and for all cows (△).

The percentage of inseminated animals reported culled because of poor fertility is shown in Figure 9. The percentage decreased from 6.0% in 1989 to 4.6% in 1996 and thereafter again increased to 6% in 2005. Heifers show lower percentages and had a somewhat different trend compared to lactating animals as they were consistently on about 3.5% from 1989 to 1998 and then increased to a high of 5.4% in 2003.

Discussion

The aim of the present study was to describe some trends in reproductive measures in Norwegian cattle the last two decades. Since NRF has been by far the most dominant breed during this period, the data presented mainly reflects the reproductive performance of this breed.
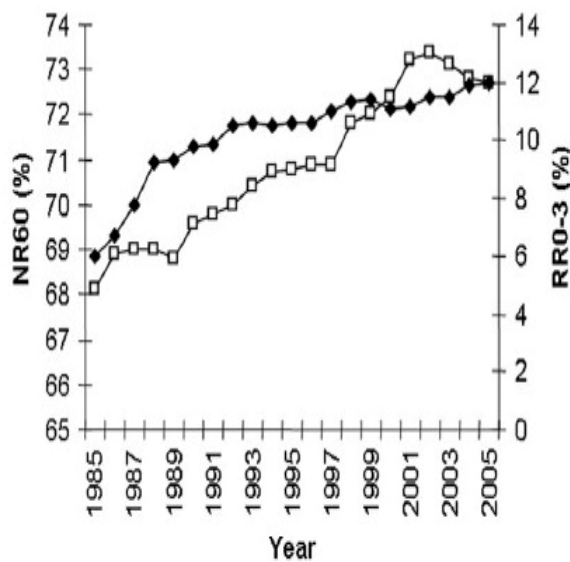
Figure 5
Sixty days non return rates (NR60, □) and return rates within 3 days (RR0-3, ◆) from 1985 to 2005.
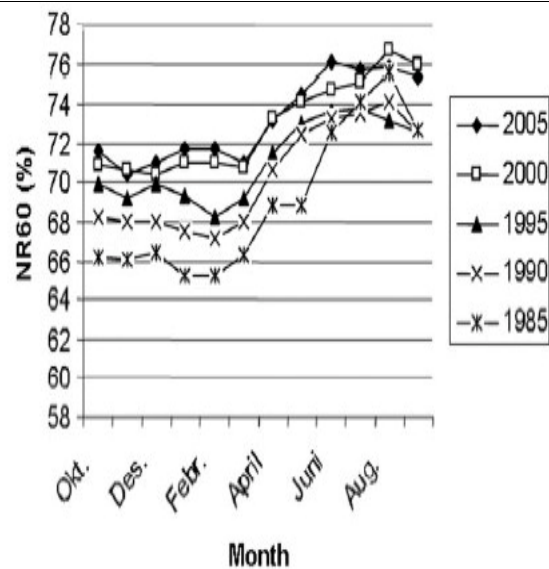
Figure 6
Sixty days non return rates by month every 5th year from 1985 to 2005.

To describe the fertility trends, 60 days non return rates and number of services per inseminated animal are used among others. As a measure of fertility, non return rates have some disadvantages, as described by Salisbury *et al*. [12]. Cows, once inseminated, may be culled, dead or bred naturally without recording, either on purpose or by accident, and appear in the records as non returns to the original insemination. On the other hand, cows that come in heat and are inseminated while pregnant will appear on the record as returns. This will also be misleading. Moreover, embryonic deaths or abortions cause some cows to return to later service even though they had conceived at an earlier one. However, when applied to large numbers of services like in this study, non return rates are considered to be very useful for studying fertility trends.
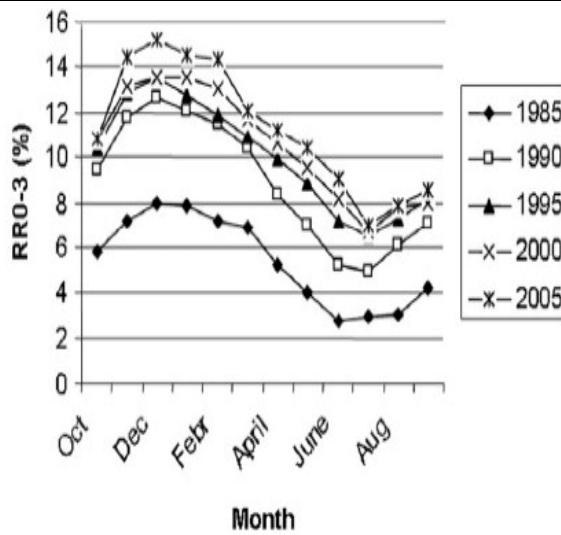
Figure 7
Return rates within 3 days (RR0-3) by month every 5th year from 1985 to 2005.
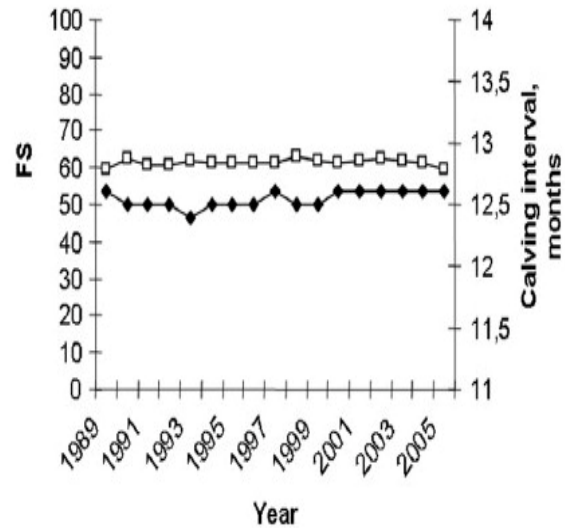
Figure 8
Average FS-index (□) and calving interval (♦) from 1989 to 2005.

The registration system in Norway is also considered to be very reliable as the inseminations are performed by technicians employed in one company, Geno (Norwegian breeding and AI-association) and by veterinarians, and both groups are paid by Geno when the inseminations are registered. Reports of inseminations being performed by herdsmen may be somewhat incomplete even though it should be done routinely according to an agreement.
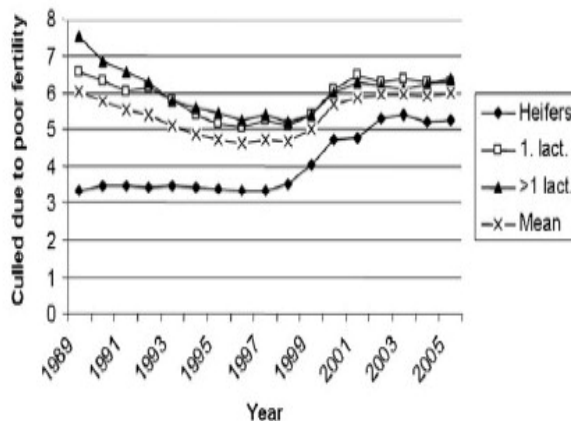
Figure 9
Percentages of inseminated animals reported culled because of poor fertility from 1989 to 2005.

However, since inseminations were not performed by herdsmen before 2002 and represent a very small part of the inseminations since then, incomplete reports from this group would be of little significance for the study. Substantially, there have been no changes in the AI reporting routines during the last decades. Therefore, the positive trend in non return rate probably reflects a true fertility improvement. This trend is in accordance with Andersen-Ranberg *et al*., studying phenotypic and genotypic trends in heifers and first lactation cows [13].

However, it is in contrast to a worldwide trend showing a decline in non return rates and pregnancy rates during the last decades, e.g. [2,5]. The non return rates in Norwegian cattle during the last decades probably also reflects a positive trend concerning pregnancy rates. Unfortunately, reliable data to confirm a close trend relationship between the two parameters have not been available so far. However, recently a Norwegian field study has indicated that the pregnancy rate is on average about 12 % lower than overall NR60 after single

inseminations [14]. In this study the overall pregnancy rate after single first inseminations in NRF was 60.7%, and the results for heifers, 1st lactation and >1 lactation cows were 68.8, 56.0 and 58.7% respectively. These results show that the pregnancy rates in NRF is relatively high when compared to studies from many other countries, e.g. [15-17].

The improvement in NR60 is probably caused by a variety of reasons, one of them being the breeding strategy, which gives increasing weight to fertility and health traits. In Norway, fertility has been emphasised in the total merit index from the 1970's based on progeny testing utilizing large daughter groups of the NRF breed [18]. Other reasons might be different campaigns and courses concerning herd management, nutrition and reproduction, routinely offered to farmers by veterinarians and agricultural advisors. The incidence rate of ketosis has decreased substantially from the mid of the 1980's [19] and this may be an effect of these activities. Reduction of ketosis may have influenced NR60 in a positive way since lowered non return rates have been found in cows treated for ketosis [20]. A successful eradication programme for Bovine Virus Diarrhoea Virus (BVDV) infection that started in Norway in December 1992 could possibly also explain some of the increase in NR60 after that time. BVDV infection is a notifiable disease in Norway, and from the start of the programme the number of restricted herds decreased from a high of 2,950 (11.3% of the herds) in 1994 to 1 by the end of 2005 [21]. BVDV infection has been associated with late return to service [22] and other reproductive disorders [23]. However, in a Norwegian study indications of a reduced conception risk were not detected [24]. From the present knowledge a possible impact of the disease on the NR60 seem to be rather small. In any case, the fact that a relatively low proportion of the herds had restrictions in the beginning of the eradication programme does not make it

likely that eradication of BVDV infection is a major cause of the increase of average NR60 that continued after the start of the eradication programme.

The increasing trend in CFI, and consequently also CLI, is probably mainly caused by managerial factors and farmer decisions. However, partly it is probably also caused by a small and undesirable genetic change for CFI, which has been observed in first lactation cows [13]. In this study, the genetic correlation between protein yield and CFI in first lactation was strongly unfavourable. There has been a considerable positive genetic change in protein yield in Norwegian dairy cattle [13]. However, the average milk yield per cow year in the period has increased from 5716 kg to 6541 kg only [9]. Genetically, the breed has a much higher milk yield potential and the relatively low yield is mainly caused by the political framework established in Norway during the period, affecting price mechanisms and feeding regimes. Thus, the system has not favoured high yields. Consequently, use of concentrates during peak lactation may have been limited leading to negative energy balance and longer interval from calving to resumption of regular cyclic ovarian activity and an increasing CFI. CFI and CLI in first lactation animals are longer than for older cows during the observation period. This is probably mainly caused by the fact that many high yielding first lactation cows are less able to meet the nutritional requirements during peak lactation and consequently need more time to resume the ovarian cyclic activity post partum and to show oestrus. However, compared to other studies, the CFI and CLI intervals are relatively short for cows in first and later lactations and the increase of the two parameters during the period studied is relatively moderate, e.g. [4,16]. Use of double inseminations is mainly caused by problems to find the optimum time of insemination. Farmers may realise that they have inseminated animals too early in oestrus and therefore order a second insemination a

day or two later. Especially farmers having strictly seasonal calving are dependent on their cows conceiving quickly and therefore may use double insemination in order to be more close to the optimum time in oestrus. The use of double insemination is more pronounced during the winter period than during summer. This may be caused by different environmental conditions, like nutritional management, photointensity and photoperiod during the winter season [25]. Using hormonal treatment to induce or to synchronise oestrus is often followed by a double insemination. This will affect the RR03 and may have caused some of the relatively rapid increase in the use of double inseminations from 1985 to 1990, just after the introduction of prostaglandins in Norway. According to the Norwegian Health Card Statistics, based on records on all milk recorded cows having their own disease journal kept in the barn [26], it was an increase in treatments of cows not observed in heat from 1980 to 1990 [19]. However, since 1990 there has been a decline in the number of such treatments without a concurrent decrease in the use of double inseminations.

The study shows that reproductive performance in Norway is consequently higher in the summer months compared to the winter season. This is in contrast to many countries under subtropical and tropical conditions experiencing decreased fertility in dairy cows inseminated during the hot summer months [27-29]. The opposite situation in Norway is probably caused by a variety of environmental factors, including climatic conditions, light intensity, nutrition (grazing versus indoor feeding) and cattle housing which is different in the relatively cold, temperate climate. Thus, summer heat stress does not seem to cause fertility problems in Norway, but cold and dark winter periods may suppress ovarian activity and oestrus expression and possibly increase embryonic mortality. However, the difference in NR60 between the highest

summer months and the lowest winter months has decreased from approximately 10% in 1985 to 5–6% in 2005 as shown in Figure 6. Increasing reproductive performance during winter over the years may be caused by a variety of factors like improved nutritional management during the indoor season and focus on exposing cattle at high latitudes during winter to dim illumination and a minimum photoperiod of 12 h [25]. Another factor may be the female fertility trait, non return rate, being selected for in NRF since 1972. This has resulted in a genetic improvement [18] and probably not least has favoured animals with a high reproductive performance during winter time. The average number of services per animal inseminated has decreased in spite of increasing use of double inseminations during the observation period. The lower number of services in heifers especially compared with 1st lactation animals, but also >1 lactation cows, is in accordance with the differences in pregnancy rates after single first inseminations registered by Refsdal *et al*. [14]. The FS-index has been fairly constant during the observation period even though the NR60 above all has increased. This is mainly caused by the fact that the average CLI interval, which has a great impact in the FS-formula, has increased. Thus, the FS-index takes into account not only the NR60 as a measure of success of insemination, but also the CLI interval reflecting the number of days open which is an economically important factor in milk production. The calving interval has also been fairly constant during the period in spite of increasing NR60 rates. This is also mainly caused by the increase in CLI interval. The percentages of inseminated animals reported culled because of poor fertility are based on information given by the farmers. This information may be inaccurate as farmers may have a different understanding of what is poor fertility, and if there is a combination of different reasons why cows are culled the primary one may be reported more or less by

chance. The decline in percentage of animals culled because of poor fertility from 1989 to 1998 is in accordance with the increasing non return rates during the same period while the ensuing increase in culling rate do not correspondingly agree with the non return rates. Per cent of culled cows discarded because of poor fertility was 12.3% in Norway in 2005 [9]. Compared to other studies this is a relatively low percentage [17,30].

Conclusion

In conclusion, most fertility measures in Norwegian cattle, mainly comprising the NRF breed, show a relatively high level of reproductive performance and a positive (NR60, NIA) or relatively constant trend (Calving interval, FS-index) during the last two decades. This is probably caused by a variety of reasons, one of them being the breeding strategy, which gives increasing weight to fertility and health traits. However, the interval from calving to first and last insemination, respectively, has slightly increased during the period and the RR0-3 has increased. The calving interval has been relatively constant in spite of increasing non return rates and lower number of services per animal inseminated, mainly because of a longer interval from calving to first insemination. This is also the main reason why the FS-index has been relatively constant. In contrast to many countries under subtropical and tropical conditions the reproductive performance in Norway is higher in the summer months compared to the winter season. This pattern has been similar over time and is probably caused by a variety of environmental factors.

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EVALUATION OF A COMMERCIAL ERNS-CAPTURE ELISA FOR DETECTION OF BVDV IN ROUTINE DIAGNOSTIC CATTLE SERUM SAMPLES

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Bovine viral diarrhoea virus (BVDV) is an important pathogen in cattle. The ability of the virus to cross the placenta during early pregnancy can result in the birth of persistently infected (PI) calves. These calves shed the virus during their entire lifespan and are the key transmitters of infection. Consequently, identification (and subsequent removal) of PI animals is necessary to rapidly clear infected herds from the virus. The objective of this study was to evaluate the suitability of a commercial Erns-capture ELISA, in comparison to the indirect immunoperoxidase test (IPX), for routine diagnostic detection of BVDV within a control programme. In addition, the effect of passive immunity and heat-inactivation of the samples on the performance of the ELISA was studied.

Background

Bovine viral diarrhoea virus (BVDV) is a widely spread cattle pathogen with a significant economic impact on cattle production [1]. The virus interferes with reproductive and immunological functions and causes subsequent losses due to reproductive disorders and impaired herd performance [2,3]. Based on phylogenetic comparison, the virus can be classified into two genotypes: BVDV-1 and BVDV- 2. Whereas BVDV-1 has a world-wide distribution, BVDV- 2 appears to be highly prevalent only in North America [4,5] and relatively rare in other continents [6,7].

The ability of the virus to cross the placenta during the first trimester of pregnancy can result in the birth of immunotolerant and persistently infected (PI) calves. These PI calves shed the virus during their entire lifespan and are the key transmitters of virus in an infected herd [8] and responsible for maintaining BVDV infections in cattle populations [9].

Consequently, identification (and subsequent removal) of PI animals is necessary to rapidly clear infected herds from the virus.

To identify PI animals, virus isolation on primary bovine cells, followed by immuno-enzyme staining is regarded as the "gold standard" method. The indirect immunoperoxidase (IPX) test is a standard method to detect BVDV in several diagnostic laboratories and is used in the BVDV control programme in Sweden [10]. During the course of this programme, the IPX test has shown to be highly effective for identifying PI animals [11,12]. However, the IPX test is time consuming and requires a high investment both in personal training and laboratory equipment, which is why antigen-capture ELISAs have been increasingly used since the early 1990's. The NS2/3-capture ELISA detects BVDV in leukocytes and tissue samples using specific affinity monoclonal antibodies (MAb) against the NS2/3 protein, and has been successfully used to identify PI animals in BVDV control

programmes in Norway and in the Shetland islands [13,14]. Recently, an antigen ELISA that uses MAbs against the Erns glycoprotein has been developed to detect BVDV. This structural protein is secreted from infected cells during virus replication and can be detected directly in serum which allows user friendly and high throughput testing and gives it the potential to be a diagnostic antigen [15, 16].

The objective of this study was to evaluate the suitability of a commercial Erns-capture ELISA (Erns ELISA; Herd- Check BVDV antigen/Serum Plus, IDEXX Scandinavia AB, Osterbybruk, Sweden.), in comparison to IPX, for routine diagnostic detection of BVDV within a control programme. In addition, the effect of passive immunity and heat-inactivation of the samples on the performance of the ELISA was studied.

Methods

1. Selection of samples

1.1. Samples from the field

In the process of virus clearance within the Swedish BVDV control programme, all calves born in infected herds are tested for virus and antibodies at an age of 12 weeks, or older. Blood samples are collected in sterile 5-ml vacutainer tubes and sent for analysis to the National Veterinary Institute (SVA), Uppsala, Sweden. From each herd detected as infected, one virus positive sample is selected for further analysis and genotyping of the infecting strain [17]. So far, only BVDV-1 has been detected in Sweden.

From samples sent in for routine diagnostics to SVA between September 2002 and February 2003, we selected 220 sera collected from 32 beef herds and 29 dairy herds throughout Sweden. According to the results from the IPX used within the routine diagnostics [18] 90 of the sera were considered virus positive and 130 virus negative. All sera were kept at -20°C until analyzed by the Erns ELISA.

1.2. Samples from PI calves with or without passive immunity

To study the influence of passive immunity on the performance of the ELISA and IPX, we selected serum samples from nine PI calves born after a previously described experimental infection of pregnant heifers [19]. In total, we tested 23 samples collected between day 0 (i.e. immediately after birth and before intake of colostrum) and day 11 post partum (Table 1). Of the nine calves, five (calves 1–5) were given colostrum free from BVDV antibodies, and four (calves 6–9) were given colostrum from their respective antibody positive dams. Antibody titres were determined in all sera using a commercial indirect ELISA (BVDV-Ab SVANOVIR™, SVANOVA Biotech AB, Uppsala, Sweden).

1.3. Heat inactivated sera

To study the influence of heat inactivation, we selected a subset of 20 sera (10 virus positive and 10 virus negative) out of the 220 samples previously selected from the routine diagnostics. Each sample was divided in two parts, and one was heat inactivated at 56°C for 90 minutes before further analysis. Heat inactivated and non-heated sera were then tested in parallel with the Erns ELISA.

2. Diagnostic methods

2.1. Detection of BVDV by IPX

The 220 samples from the field and the 23 samples from PI calves were also tested for BVDV by IPX. The test was carried out on 96-well plates using low-passage bovine turbinate cells. Serum (20 μl) was added to each of four wells before the addition of 100 μl of cell suspension. Positive and negative control sera were run on each plate. The test plates were incubated for 4 days in 5% CO_2, 37°C. Plates were fixed and dried, then stained with immunoperoxidase as described by Meyling [18], using a polyclonal bovine anti-BVDV serum (BVD virus positive control serum, VLA, Weybridge, UK) to detect the virus. The presence of red-brown cytoplasmic staining in any of the wells exposed to the specific anti-BVDV antibody denoted a positive result.

Table 1. Results from testing for BVDV in sera collected between days 0 and 11 post partum from nine PI calves born after experimentally infected heifers, using a commercial Ernscapture ELISA (HerdCheck BVDV antigen/Serum Plus, IDEXX Scandinavia AB, Osterbybruk, Sweden.) and the indirect immunoperoxidase test (IPX).

PI calf no.	Age (days)	Antibody titre	Virus detection IPX	Erns ELISA[a]	(COD)
1	0	<1:10	-	+	(3.32)
	2	<1:10	+	+	(2.96)
	7	<1:10	+	+	(2.70)
2	0	<1:10	+	+	(2.99)
	2	<1:10	+	+	(3.52)
	3	<1:10	+	+	(3.42)
3	0	<1:10	-	+	(3.21)
	2	<1:10	+	+	(3.00)
	7	<1:10	+	+	(2.97)
	11	<1:10	+	+	(2.52)
4	0	<1:10	+	+	(3.33)
5	0	<1:10	-	+	(3.56)
	2	<1:10	+	+	(3.26)
6	0	<1:10	+	+	(3.27)
	2	1:250	-	-	(0.16)
	5	1:250	-	+	(3.29)
	7	1:10	-	+	(3.28)
7	2	1:250	-	+	(0.48)
8	4	1:1250	-	-	(0.29)
	6	1:250	-	+	(1.58)
9	2	1:1250	-	+	(2.92)
	7	1:1250	-	-	(0.04)
	9	1:1250	-	-	(0.07)

Calves 1–5 were given colostrum free from BVDV antibodies, and calves 6–9 were given colostrum from their respective antibody-positive dams. Samples collected day 0 were taken before intake of colostrum. BVDV antibody titres were determined using a commercial indirect ELISA (SVANOVA Biotech AB, Uppsala, Sweden) in dilutions 1:10–1:1250.

[a] Samples with COD > 0.30 as measured by the Erns ELISA were considered positive

2.2. Detection of BVDV by antigen ELISA

All samples were tested for BVDV antigen using the Ernscapture ELISA according to the manufacturer's instructions. Briefly, provided detection antibodies were added to all wells of a microtitre plate wells coated with Erns MAbs. Positive and negative control sera were added to appropriate duplicate wells, and the serum samples (50 µl) then added to the remaining wells. The plate was incubated for 2 hours at 37°C, before washing and addition of conjugate and substrate. The optical density values (ODs) were measured at 450 nm, and the corrected optical densities (CODs) of samples and positive control then calculated by subtracting the mean OD for the negative controls from obtained OD (COD = ODobtained – mean ODnegative controls).

Samples with COD> 0.30 were classified as positive.

2.3. Detection of antibodies

The antibody titres of the sera from the nine PI calves were determined using the commercial indirect ELISA in dilutions 1:10 to 1:1250. The ELISA was performed according to the instructions of the manufacturer. The COD values from the indirect ELISA (CODAb) were calculated before interpretation of the result by subtracting the OD for control antigen from obtained OD (CODAb = ODobtained - ODcontrol). Antibody titres were determined as the highest dilution with CODAb ≥0.2.

3. Statistical analysis

The sensitivity (Se) and specificity (Sp) of the Erns ELISA were calculated in relation to the IPX test, and the degree of agreement between the tests was estimated by the kappa (*k*) ratio. To estimate the effect of heat inactivation on the performance of the ELISA we evaluated the repeatability of the test before and after heat inactivation of the samples using the concordance correlation coefficient (CCC) [20] and Bland-Altman plot [21].

Results

Samples from the field

The results from the testing of the 220 sera, selected among samples sent in to SVA, are summarized in Table 2. All 130 samples categorized as virus negative by IPX were tested negative in the ELISA, and all 90 samples categorized as virus positive were tested positive, i.e. the relative Se and Sp of the ELISA was 100% in relation to IPX, and the agreement between the tests was perfect (*k* = 1.0). The frequency distribution of COD values can be seen in Figure 1. Out of 90 samples considered as virus positive according to the IPX test results, 89 had COD values well above the cut-off (>1.2).

Samples from PI calves with or without passive immunity

The results of the testing of the 23 samples from PI calves are given in Table 1. Out of 14 samples with antibody ELISA titres < 1:10, 14 were tested positive in the Erns ELISA and 11 in the IPX. The three samples that were falsely classified as negative by the IPX were all collected day 0 post partum, i.e. before intake of colostrum. Among the 9 samples with antibody titres ranging between 1:10 and 1:1250, 5 samples were tested positive in the Erns ELISA and none in the IPX.

Heat inactivation

The agreement between results obtained before and after heat inactivation can be seen in Figure 2. There was a perfect agreement of the interpretations of the test results obtained before and after heat inactivation, and the CCC was calculated to 0.99. The BA plot (not shown) indicated that 95% of the differences between heat-inactivated and non-heated samples fell in the range of -0.39 and +0.22 units.

Discussion

The identification of PI animals (for subsequent elimination) is an essential element in any BVDV control programme, and depends on accurate diagnostic tests, i.e. tests with high sensitivity and specificity that have been thoroughly evaluated for routine diagnostic use. Moreover, for testing of large series of samples it is desirable that a test is user friendly and allows automation. Even though the IPX test currently used in Sweden has shown to be efficient for detection of PI animals, it is evident that the Erns ELISA have several advantages: it is independent of cell cultures, gives a test result within a few hours and is relatively inexpensive both to establish and run [22]. In addition our results clearly demonstrate that it performs well
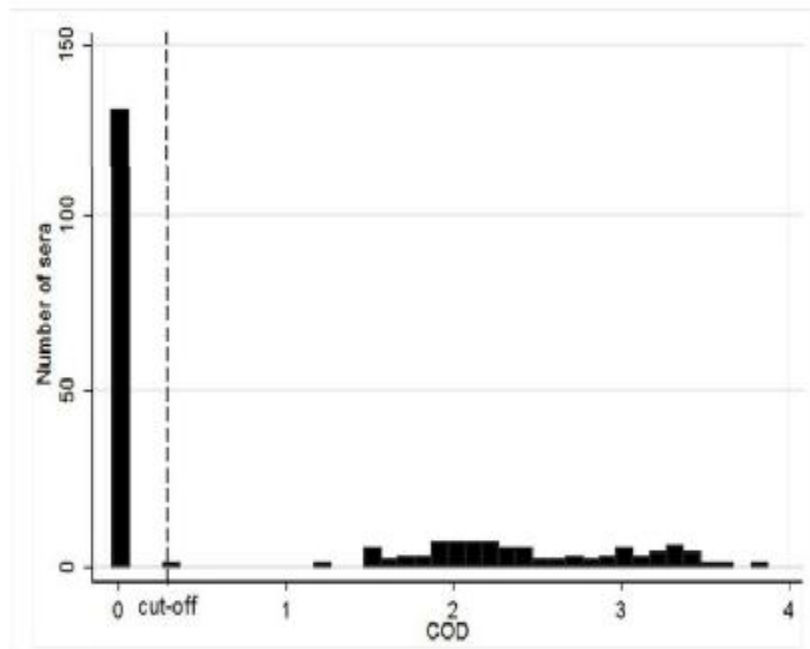
Figure 1

Frequency distribution diagram of corrected optical density (COD) values as measured by a commercial E^{rns}-capture ELISA (HerdCheck BVDV antigen/Serum Plus, IDEXX Scandinavia AB, Österbybruk, Sweden) in 90 bovine sera considered as virus positive and 130 bovine sera considered as virus negative according to the indirect immunoperoxidase test used within the Swedish BVDV control programme. All sera were selected among samples sent for routine diagnostics to the National Veterinary Institute, Uppsala, Sweden, between September 2002 and February 2003. ELISA results with COD > 0.30 were considered positive.

under Swedish conditions, i.e. for detection of BVDV-1, and that its performance is comparable with the IPX test. There was a perfect agreement between the results from the two tests, and the separation between COD values from negative and positive samples was good. Out of 220 samples, 219 had COD values either well below or well above the cut-off. However, one sample, considered as virus positive according to the IPX test results, had a COD value close to the cut-off, and there are a number of possible explanations for this result. Firstly, as with the majority of BVDV antigen ELISAs, this Erns ELISA has been developed for the identification of PI animals. Whereas virus titres in PI animals normally range between 102.2 and 106 TCID50/ml, titres during transient infections have been reported to be as low as 100.9 [23-25]. It is likely that the detection level of the IPX test is lower than that of the ELISA, and it is possible that this serum sample originated from a transiently infected animal. Secondly, although PI animals normally have high virus titres, these may, as previously mentioned, show a wide range. Consequently, it is also possible that this serum sample originated from a PI animal, but that the virus titer was low, and close to the detection limit of the ELISA.

Note: Data must overlay dashed line for perfect concordance
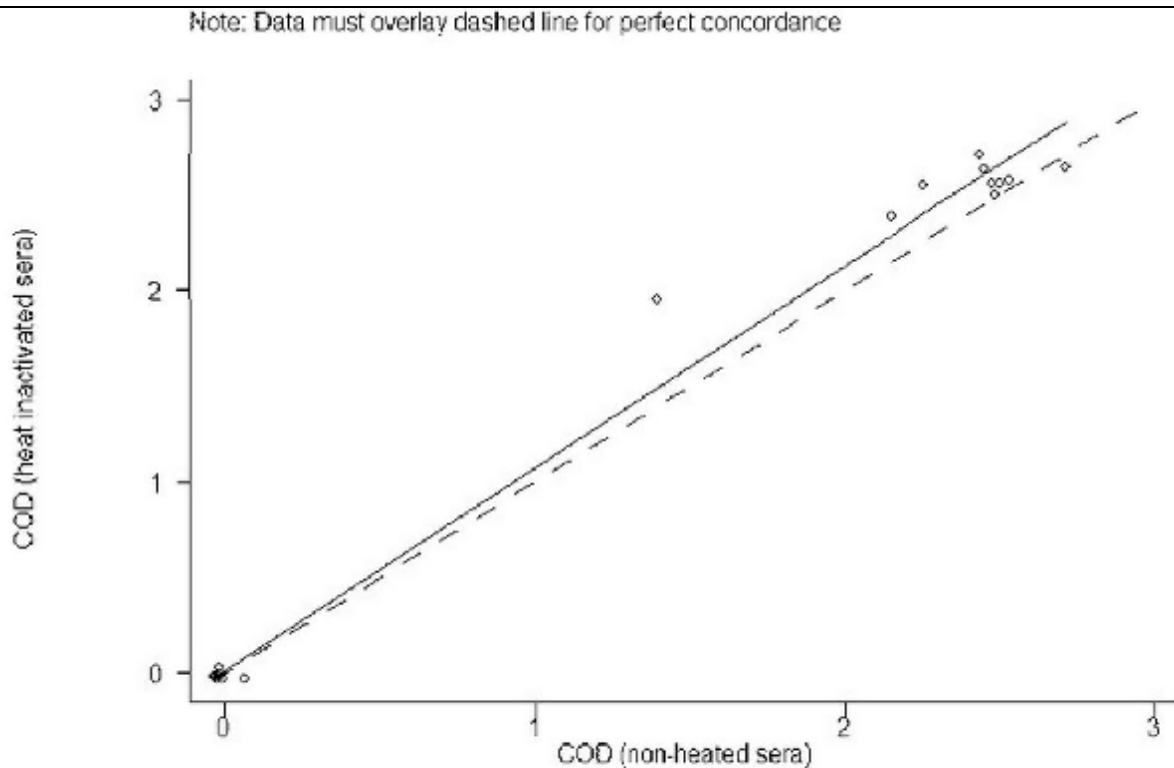
Figure 2

Agreement between COD values obtained with a commercial E^{rns}-capture ELISA (HerdCheck BVDV antigen/Serum Plus, IDEXX Scandinavia AB, Österbybruk, Sweden.) from testing of 20 bovine serum samples (10 virus positive and 10 virus negative) before and after heat inactivation at 56°C for 90 minutes (CCC = 0.99).

Because the Erns ELISA, unlike the IPX test used, is based on MAbs and has been developed and validated for detection of BVDV-1 and BVDV-2, it is probably not as broadly reactive as the IPX. It has been shown not to detect some closely related border disease virus strains [26], and may, consequently, also miss atypical pestiviruses. This should be kept in mind, as there are indications that atypical pestiviruses are already circulating in cattle populations[27,28].

It was demonstrated that both tests might fail to detect a large proportion of PI calves in the presence of persisting maternal antibodies, confirming results from previous studies[29,30]. However, whereas the IPX test gave false negative results also in the presence of low antibody titres, the Erns ELISA detected BVDV in three out of four sera with antibody titres up to 1:250, indicating that the Erns ELISA is less influenced by passive immunity. We could also observe that the IPX test, unlike the Erns ELISA, gave false negative results in three out of five newborn PI calves sampled before intake of colostrum. This has been observed previously and is hard to explain (Ronsholt, personal communication), but is one of several reasons for which precolostral sampling is not practiced within the Swedish BVDV control programme. In addition, it was demonstrated that the performance of the Erns ELISA was not influenced by heat inactivation, which can be an advantage in laboratories where sera are often subject to several analyses and therefore heat-inactivated by routine.

Conclusion

Based on these results we can conclude that the Erns ELISA is a valid alternative to the IPX test. It is highly sensitive and

specific, can be used for testing of heat-inactivated samples, precolostral testing, and probably to detect PI animals at an earlier age than the IPX. However, it should be kept in mind that this ELISA, unlike the IPX, uses MAbs, and that it therefore is less likely to detect atypical pestivirus strains.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

JK and SA took part in all aspects of the study, including study design, laboratory analysis, interpretation of the results, and drafting of the manuscript. KS participated in interpretation of the results and drafting of the manuscript. LR participated in study design and revision of the manuscript. All authors have read and given final approval of the version to be published.

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THE CONNECTION BETWEEN LIPID PEROXIDATION AND THROMBIN-FIBRINOGEN INTERACTION
(message I)

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While modeling experimental conditions with accelerated or inhibited process of lipid peroxidation in thrombocytes (rat tests), it was shown that acceleration of continuous intravascular blood curtailing is supervened upon hyperoxidation, thrombin-fibrinogen interaction plasma markers' value being controlled. The same was seen among patients with insulin-dependent diabetes, basedowians, prostate gland adenoma, persons with atherosclerosis of lower limbs arteries, women with physiological pregnancy and the pregnancy complicated with eclampsia and the pregnant after cesarean section.

Between lipid peroxidation intensity in thrombocytes and the rate of intravascular blood curtailing, a very close to linear direct dependence was detected. Using a complex antioxidant, selmevit, alongside usual therapy, restricts lipid peroxidation and continuous intravascular blood curtailing acceleration, and thus, a thrombotic complication hazard.

Taking into account the dependence of many life-support systems from lipid peroxidation (LPO), its changes at some physiological and pathological conditions [1, 2, 3], the data about the connection between hemostasis and LPO [4], the supposition according to which this connection is realized by blood platelets [5], we have studied the dependence between the intensity of thrombin-fibrinogen (ITF) and lipid peroxidation (LPO) interaction in blood in various experimental and clinical situations, hoping, that it will allow to estimate the role of lipid peroxidation in hemostatic potential maintenance and the possibility of the direct influence on intravascular clotting (inopexia) (IVC) – the process going on continuously in physiological conditions [6, 7, 8].

In experiences on rats changes of ITF products value (soluble fibrin monomeric complexes - SFMC, products of fibrin degradation - PFD, D-dimers, P_3 and P_4 factors, general blood coagulability, platelet value, their general coagulant activity,

spontaneous and ADP-induced aggregation) when introducing LPO inhibiting compounds (mercasolil , 6-methyluracil, a complex of oxidation preventive vitamins - selmevit, a synthetic antioxidant dimephosphon), and also the LPO activating compounds, (lead, thyroxin, sex steroids) were studied. Alongside with it, the LPO and ITF changes when being affected by primarily accelerating or slowing down the ITF factors (heparin and adrenaline injections, blood loss, seasonal factors) were evaluated. For the estimation of the ITF markers level, platelet aggregation and the LPO rate displays, well known methods were used [9, 10, 11]. In some experiments the tests were selected with small intervals to estimate the sequence of hemostasis and lipid peroxidation shift occurrences.

The data about positive influence of oxidation preventive vitamins on hemostasis having been obtained, the ITF rate among patients suffering from the diseases which are usually accompanied with

hyperoxidation, was clinically studied, the LPO being preliminary activated; applying usual therapy or the same therapy added by a complex of antioxidants - selmevit. Patients with insulin-dependent diabetes, basedowians, prostate gland adenoma before and after the operation (strumectomy or adenomectomy accordingly), persons with atherosclerosis of lower limbs arteries, women with physiological pregnancy and the pregnant with eclampsia before and after easy delivery or after cesarean section were examined.

Analyzing the results of experimental observations continued more than 15 years, we have received the bases for ascertaining of some positions:

1.The introduction of various biologically active compounds accelerating LPO (ethinylestradiol, levonorgestrel, thyroxin, lead) to experimental animals (white rats), increases the value of direct and indirect ITF markers in blood. The introduction of LPO inhibiting compounds (selmevit, complivit, dimephosphon, arachidonic acid paralyzers – mepacrin, aspirin and dasoxiben) causes the opposite effect.

2.When the hemostasis activating compounds or those leading to its activating (adrenaline, blood loss, low temperature of the environment, seasonal factors) introduced, alongside with the growth of ITF markers value, the LPO rate is increased. The ITF slowing down influences (the introduction of heparin, pelentan) weakens the LPO process intensity.

3.The introduction of LPO accelerating compounds (lead, sex steroids, thyroxin), simultaneously with antioxidants (selmevit, dimephosphon) inhibits or excludes the LPO activation and the ITF markers' value growth.

4.By physiological and pathological conditions (texis, puerperal period, the pregnancy complicated with eclampsia, cesarean section, atherosclerosis of lower limbs vessels with ischemia, toxic goiter, prostate gland adenoma), which are characterized with hyperoxidation and shifts in hemostasis (general high coagulability of blood and platelet coagulation activity), the ITF markers' value in plasma of blood increases.

5.The addition with antioxidants of the usual therapy used at these diseases, inhibits the LPO intensification and antioxidant thrombocyte potential decrease, and reduces the hemostasis condition showers' restoration period up to the amounts peculiar to healthy donors.

6.The LPO acceleration in thrombocytes precedes the platelet coagulant activity shifts and the ITF markers level, different by nature and properties compounds capable to cause hyperoxidation, affecting; confirming the role of thrombocytes in realization of the connection LPO-HEMOSTASIS.

The connection between LPO and ITF, hence, and the connection of LPO with continuous intravascular blood curtailing, is carried out through thrombocytes: LPO changes in these cells precede their coagulant activity shifts, and this, in its turn, precedes ITF acceleration. The proof of close connection between lipid peroxidation and intravascular blood curtailing is close to linear character of dependency between lipid peroxides value in thrombocytes and the ITF markers value in blood plasma (at the graphic analysis of LPO and ITF dynamics, the dependence between them is close to linear one and excels with a high approximation coefficient, approached to one - from 0.9867 up to 0.9987). In particular, lipid peroxide growth level and antioxidant potential decrease in thrombocytes, the release reaction acceleration of P_3 and P_4 factors and spontaneous platelet aggregation, their general coagulant activity growth, ITF acceleration attributes (SFMC, PFD and D-dimers value growth), are supervened upon a thyroxin injection. Thus, the factors changing LPO intensity, realize the influence on ITF through thrombocytes activation.

Taking into consideration the existence of bilateral dependence between thrombinemia and platelet activity [12], and also the data, indicating the bilateral dependence LPO ↔ hemostasis [13], it is possible to express the idea in the form of a closed cycle:

hyperthrombinemia ® LPO activation in thrombocytes ® hyperthrombinemia (the cycle is closed)

The data about the sequence of changes in time allow to detail this scheme, having included in it also the results of ITF intensity supervision, estimated upon the markers of the process:

LPO activation (or inhibition) in thrombocytes being affected by prooxidants (antioxidants)
E
Platelet coagulant activity increase (or decrease)
E
Acceleration (or limitation) of thrombin and fibrinogen interaction

Such representation testifies the expediency of the research continuation aimed at profound studying of shifts' dynamics at pathological conditions, proceeding with the hyperoxidation phenomena.

We document the generalizations resulted here in messages II-VI with decoding of experimental schemes and the fact sheet.

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PROMPT EFFECTIVE CORRECTION OF THROMBOCYTE HEMOSTASIS DIATURBANCES IN NEW-BORN CALVES WITH DYSPEPSIA

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1. Phosphopag, acos and calcium gluconate complex application in new-born calves with dyspepsia normalizes lipid peroxidation and MM content in their blood and thrombocytes.

2. Phosphopag, acos and calcium gluconate application during 10 days in new-born calves with dyspepsia normalizes the condition of the estimated indicators of primary hemostasis, optimizing thrombocyte aggregation and blood platelets' intravascular activity.

Trombocyte hemostasis alterations in new-born calves with dyspepsia cause the development of intravascular thrombosis. Primary hemostasis activation on dyspepsia mostly depends on lipid peroxidation (LP) increase in animal' organism that activates thrombocyte aggregation increase mechanisms. The ways of prompt and effective correction of thrombocyte functional condition in calves with dyspepsia completely excluding the risk of thrombosis still have not been worked out.

Phosphopag (Polyhexamethylenguanidine phosphate), new biologically active preparation can effectively arrest dyspepsia in new-born calves and is being actively tested now [4]. Much attention is paid to economically available sorbent acos (hydroaluminum silicate from Belgorod region fields). Calcium gluconate is used to stimulate the calves' gastric secretion. The combination of phosphopag, acos and calcium gluconate has been supposed to completely correct thrombocyte function in new-born calves with dyspepsia.

The aim of the research is to find the possibility of prompt effective correction of thrombocyte hemostasis in new-born calves with dyspepsia with the help of the combination of phosphopag, acos and calcium gluconate.

Materials and methods

Research group is represented by 26 new-born calves with dyspepsia. The sick calves had all the symptoms of dyspepsia with clear intoxication. The control group consisted of 267 healthy new-born calves. The examination comprised the reveal of lipid peroxidation (LP) activity of plasma by the content of TBA-active products with the help of the tool kit of LLC "Agat-Med". Antioxidant potential of liquid part of blood was estimated [1]. Thrombocyte lipid peroxidation was defined by the concentration of basal level of malonic dialdehyde (MDA) in reducing reaction of thiobarbituric acid [7], in modification [3]. The level of medium molecules (MM) was defined in plasma and in resuspended thrombocytes [2]. The thrombocyte amount in capillary blood was calculated in Gorjaev's chamber. The thrombocyte aggregation (TA) was examined by means of visual micromethod [6] using ADP $(0,5 \times 10^{-4}$ M), collagen (the basic suspension dilution 1:2), thrombin (0,125 unit/ml), Ristomycin (0,8 mg/ml) (NPO "Renam"), adrenalin $(5 \times 10^{-6}$ M., Gedeon Richter factory) as inductors and using the combination of ADP and adrenalin, ADP and collagen, adrenalin

and collagen to model the real blood flow condition. Intravascular thrombocyte activity (ITA) was defined with the help of phase-contrast microscope [5] according to Shitikova A.S. and co-authors (1997). According to the bottle-feeding schedule the 26 calves were prescribed to take 100,0 ml of 0,01 % phosphpag in the morning, 10 % 10,0 of calcium gluconate in the afternoon and 150 mg of acos per kg of live weight during 10 days. Statistical treatment of the results achieved was carried out using Student t-criterion.

The results of research

The increase of lipid peroxidation was observed in new-born calves with dyspepsia. TBA-active products concentration in plasma was 5,16±0,12 micromole/l, in control group – 3,92±0,06 micromole/l. Plasma antioxidant activity of sick animals was reduced (21,2±0,06 %), in control group – 28,6±0,04 %. The revealed MDA increase in thrombocytes (1,66±0,001 $nmole/10^9$), and in control group – 0,89±0,02 $nmole/10^9$) was the evidence of free radical oxidation (FRO) caused by the reduction of thrombocyte antioxidant activity. Medium molecules' levels in plasma came to MM_{280} – 0,52±0,04 standard units, MM_{254} – 0,35±0,02 standard units, medium molecules amount in thrombocytes MM_{280} – 0,065±0,02 standard units $/10^9$, MM_{254} – 0,072±0,01 standard units/10^9, which are authentically higher than control indexes.

The calves' treatment with the combination phosphopag, acos and calcium gluconate had positive effect on plasma and thrombocyte lipid peroxidation. TBA-active products amount in plasma reduced (P<0,01). By the 10th day of treatment their concentration was 3,97±0,05 micromole/l. Lipid peroxidation products reduce lead to normalization of plasma MM_{280} up to 0,32±0,09 standard units, MM_{254} – 0,23±0,06 standard units. Lipid peroxidation products reduction in plasma was accompanied by the reduction of MDA basal level in thrombocytes after the 10th day of treatment

(0,90±0,03 $nmole/10^9$). The calves' treatment with the combination of phosphopag, acos and calcium gluconate lead to normalization of MM level in trombocytes MM_{280} – 0,050±0,06 standard unit/10^9, MM_{254} – 0,054±0,01 standard unit/10^9.

Thrombocyte content in the sick calves' blood was normal before and after treatment. TA increase was revealed in calves with dyspepsia before treatment especially under the influence of collagen (20,3±0,05 c). TA developed slower in sick calves under the influence of ADP (36,0±0,10 c) and Ristomycin (31,6±0,02 c). Thrombin (43,6±0,22 c) and adrenalin (82,0±0,03 c) TA were revealed later on but developed quicker than in control group (P<0,01). The time of TA development under the influence of the inductors' combination treatment was also accelerated (ADP+adrenalin – 22,0±0,05 s, ADP+collagen – 20,0±0,01 s, adrenalin+collagen –19,0±0,02 s).

On prescribing the combination of phosphopag, acos and calcium gluconate TA time increased under the influence of all inductors. Collagen turned out to be the most active TA inductor by the 10th day of treatment (31,0±0,05 s). ADP (39,0±0,05 s), Ristomycin (41,0±0,12 s) were less active. TA developed still slower under the influence of thrombin and adrenalin. On the inductors combination TA time increased (ADP+adrenalin - 36,0±0,03 s, ADP+collagen – 27,0±0,05 s, adrenalin+collagen – 30,0±0,05 s).

Thrombocyte intravascular activity in calves with dyspepsia was characterized by its' increase. Discocyte level in sick calves' blood was 62,3±0,06 % (in control group – 82,0±0,16 %). Disco-echinocyte content has increased 1,60 times. The amount of spherocytes and sphero-echinocytes was also bigger than control data (13,2±0,04 % and 6,8±0,05 %, correspondently). The total thrombocyte active forms amount (37,7±0,02 %) in sick calves has increased 2,09 times. The large and small aggregates content in the blood was 4,5 and 45,8 times higher

correspondently than in control group, and thrombocyte amount in sick calves' aggregates was 2,8 times higher than in control group.

Phosphopag, acos and calcium gluconate combined treatment for calves with dyspepsia has allowed to achieve positive ITA dynamics. Real ITA indicators improvement was revealed by the 10th day of treatment. Since phosphopag, acos and calcium gluconate combined treatment discoid thrombocytes content in sick calves blood has increased up to 82,3±0,6 %. As a result of treatment the disco-echinocyte, spherocyte and sphero-echinocyte levels in sick animals blood really decreased (9,4±0,01 %, 4,6±0,05 % and 2,7±0,3 %, correspondently). Since phosphopag, acos and calcium gluconate combined treatment the total amount of thrombocyte active forms has become close to that in control group (17,7±0,04 %). The large and small aggregates amount by the 10th day of treatment has decreased 4,37 and 36,6 times correspondently. Thrombocytes amount in the aggregates has become 5,0±0,09 %.

Discussion.

Increased lipid peroxidation in plasma and thrombocytes of calves with dyspepsia reveals the reduction of their organisms' antioxidant system [1] and causes MM level increase in plasma and thrombocytes. Lipid peroxidation normalization and antioxidant plasma potential on MM reduction as a result of the treatment reveals the normalizing effect of phosphopag, acos and calcium gluconate combined treatment on new-born calves with dyspepsia homeostasis. This is the result of all preparations' effect on metabolism and the increase of the organism antioxidant system enzymes expression.

The estimated homeostasis indicators normalization on phosphopag, acos and calcium gluconate combined treatment reveals its' positive effect on thrombocyte hemostasis realization mechanisms in new-born calves with dyspepsia. This is no doubt explained by the metabolism processes improvement, the reduction of lipid peroxidation and MM toxic effect in plasma and thrombocytes along with the optimization of the process of exogenous signals reception by the thrombocytes. Thrombocyte aggregation activity corresponded to that in control group in new-born calves with dyspepsia being treated with phosphopag, acos and calcium gluconate during 10 days.

Normalization of TA duration in new-born calves under the influence of Ristomycin, and being treated with phosphopag, acos and calcium gluconate, is the evidence of optimization of concentration in blood adhesive molecule i.e. von Willebrand Factor.

Total ITA normalization enables to minimize the thrombocyte complications risk in new-born calves with dyspepsia being treated with phosphopag, acos and calcium gluconate. High effectiveness of the treatment carried out in thrombocyte hemostasis correction in new-born calves with dyspepsia enables to recommend the preparations' combination under research to be widely adopted in live farming.

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Materials of the Conferences

THE INFLUENCE OF ELECTROMAGNETIC FIELDS ON THE RATE OF AGEING OF THE WORKERS IN THE REGION OF KURSK MAGNETIC ANOMALY

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Different electromagnetic fields (EMF) are widely distributed and used in industry, science, engineering and medicine. Some electromagnetic factors are potentially dangerous for human organism, such as the Earth's natural magnetic field, constant EMF, alternating EMF from 1 Hz to 300 GHz, especially it is distinguished EMF with industrial frequency (50 Hz) and EMF with the frequency from 10kHZ to 20 GHz.

Now the population of many countries is exposed to electromagnetic waves with the physical characteristics of industrial EMF. It determines the topicality and importance of the integral assessment of the environmental and occupational EMF influence on the health of people in general and of the workers in different brunches of industry.

Acute or chronic organism affection depends on intensity and duration of EMF exposure.

Acute damages develop as a result of the serious violation of the safety precautions (sanitary-hygienic standards) or in industry accident. Chronic disturbances manifest by astenic, astenovegetative syndromes, peripheral angiovegetative syndrome, abnormalities in gonad gland function etc. The remote signs of the affection are early development of atherosclerosis, ischemic heart disease, arterial hypertension, vascular encephalopathy, oncology processes, Alzheimer illness etc.

Kursk magnetic anomaly (KMA) is the region near city Kursk and unique territory in the Earth with abnormal high level of natural Earth's magnetic field. It is linked with the great amount of iron-ore in underground. Intensive development of ore extracting and ore processing industry are associated with the increase of exposure to diverse EMF, at first – due to uncovering of the layers of magnetic ore and at second – as a result of using the ore concentration technique with the considerable generation of artificial electromagnetic waves (magnetic separators).

The scientific researches of M.P.Travkin with co-authors (1969), A.A.Plemenov with co-authors (1990), V.V.Belskij and P.V.Kalutskij (1997), A.M.Chernich (2004) proved that prolonged exposure of EMF in KMA is the serious risk factor for the health of the people living in this region and especially, working in the local ore mining and ore processing.

Our previous investigations revealed that different occupational harmful factors led to the abnormalities in systemic organization of the organism function, provoke the general and occupational diseases and therefore premature ageing (V.I.Babkina, A.V.Zavialov, 2005). The interrelation of premature ageing with influence EMF of various frequency is established in investigations of scientist's research institute of Medicine of labour of Russian Medical Science Academy (N.F.Izmerov and co-authors, 2001-2006) and Kursk state medical university (N.K.Gorshunova and co-authors, 2005).

The influence of EMF in Kursk magnetic anomalous territory on the ageing is still unknown.

The aim of this research is to define the rate of ageing among workers exposed to diverse EMF in KMA for the substantiation of the principles of the assessment of the work ability and occupational suitability of the industrial workers.

Seventy one men lived in KMA and engaged in the local ore mining and ore processing enterprise (the basic group) and seventy workers of rubber production plant (Kursk city)(the control group) were examined. Both groups had no considerable differences in the patient's age (50,5±1,7 years) and total work experience (24,2±0,9 years). All workers contacted at workplace with similar harmful industrial factors (dust, noise and vibration exceeding top permitted level). Control group consist of persons living and working in normal natural magnetic field' conditions. The persons of the experimental group which had been living in

natural anomalous region more then 20 years were divided into two subgroups. The first subgroup included the workers of open-cast mine (they contacted with the uncovered magnetic ore), the second subgroup consisted of the operators, which serviced magnetic separators (the source of industrial EMF).

The general (BA) and proper biological age PBA has been defined by the method of V.P.Voitenko et al., 1984 as the integral index of the functional state in dependence on age-related disturbances. The difference between BA and PBA determined the rate of the person ageing. The significance of it is equal ± 5 years estimated as physiologic (normal) ageing, more then 5 years - accelerated ageing. The delayed ageing was characterized by the low level of BA (proper BA was considerably more then BA).

Rates of ageing at workers of experimental group have made 13,4±1,8 years, and were authentically above, than in control group (7,1±0,4 years; p<0,05). At quarry' workers and the persons serving magnetic separators of concentrating factory, authentic differences in rates of ageing it is not revealed: accordingly 15,3±2,9 years and 12,1±1,6 years.

59% workers from experimental group and 11% workers of rubber production plant had premature rate of ageing. 64,5% of quarry' workers and 55% of men serving magnetic separators had accelerated rate of ageing.

The most frequent pathology was arterial hypertension (AH) in the both workers' groups (35% workers from the ore concentrating factory, 16,1% from quarry' workers). Only 12% workers in control group suffered AH. Majority of workers (83%) had the premature ageing.

Conclusion. Prolonged exposure of abnormal natural magnetic field and industrial EMF in KMA region often lead to the acceleration of ageing processes. One of the main reasons of worker's premature ageing was AH.

PRIORITY OF GLUTATIONPEROXIDASE AND GLUTATIONTRANSFERASE ACTIVITY CHANGES AT CHRONIC ADENOIDITIS AND THEIR REVERSIBILITY

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High percentage of chronic adenoiditis (CA) among children, comparative resistance, and, in vivid cases, – little reversibility of the pathological process afflicting almost only children, - all this adds great significance to the problem of CA prophylaxis and treatment.

Aim: testing the state of antioxidant system at chronic adenoiditis among children, the optimization of remedial measures.

Materials and Methods: during randomized, prospective, controlled, simple blind clinical research the content of cytosolic enzymes of the antioxidative system – superoxide dismutase (SOD), catalase, glutationperoxidase (GPO) and glutation-S-transferase (GST) in the erythrocytes of 72 children with authentic diagnosis 'chronic adenoiditis' before and after care with a complex homeopathic preparation "Tonsilotren" (DHU, Germany). The control group consisted of 16 donors who had no chronic, somatic or ENT-pathology in the anamnesis and hadn't got any drug therapy for the previous month because of acute respiratory viral infection or any other nosology.

Results: GST enzymes' activity decrease ((1,100±0,118) mmol/min*ml cells (P<0,05)) and GPO ones' ((4,36±1,00) mmol/min*ml cells (P<0,05)) in erythrocytes of the children with chronic adenoiditis was established, that affords ground for supposing their priority at the given nosology. The results of SOD and catalase activity in the erythrocytes had no authentic differences.

The reversibility of the showings after the therapy with "Tonsilotren" reflects functional recovery activity of the enzymatic antioxidative system when the adaptation tension at chronic adenoiditis is developed.

Conclusions: the confirmation of the biochemical aspects of pathogenesis of chronic adenoiditis among children and the possibility to correct them has outlined the perspectives of pathogenetic therapy. The GPO and GST correction against the background of complex homeopathic preparation "Tonsilotren" is an indirect predictor of its efficiency. The specified fact gives us title to work out not only a pathogenically new method of care of chronic adenoiditis, but also rehabilitation programs during the remission period, that is in accord with the principals of immune rehabilitation at chronic infective inflammatory diseases.

DYNAMICS OF LATE COMPONENT OF BLINK REFLEX AMONG PATIENTS WITH HYPOTHYROIDISM

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Physiological effects of thyroid hormones are spread practically onto all aspects of an organism's vital activity. Being under the controlling influence of direct and humorally mediated nervous impulses the thyroid gland, in its turn, affects formidably the processes occurring in different levels of the nervous system. There are the data about a greater sensibility of nervous processes to thyroid hormones compared to those occurring in other tissues of the body. This is known to become apparent especially on the early stages of ontogenesis.

The importance of studying of motor disorders' nature question at the deficit of thyroid hormones circulating in the body was underlined by many clinicians and pathophysiologists. The nature of dyskinesia at hypothyroidism was regarded by different authors according to two main concepts about the mechanism of thyroid hormones' action – immediately on the muscular tissue or nervous system-mediated.

While considering the effects of thyroid hormones in the whole body, one should take into account the multiplicity of their action's application points, and first of all their influence on the majority of tissues' metabolism. On this basis it is hardly correct to restrict the nature of motor function's disorders at hypothyroidism to soft tissue involvement only. The morphological research showed that there are authentic proofs both for the first and the second points of view.

Movement control is a complex coordinated influence of different levels of nervous system on the end-point organ of motor apparatus – muscles. The deficit of thyroid hormones affects the function of nervous centers, and that can't help playing a significant role in the nature of locomotion disorders.

Until present time the question of the functional state of over-segmental brain parts at hypothyroidism is being open. Meanwhile these data can be of concern for understanding dyskinesia pathogenesis at thyroid gland diseases.

Our work was aimed at studying clinic and neurophysiologic characteristics of reflex action of the neuromotor system among patients with hypothyroidism. To do it we examined 20 people with primary hypothyroidism. 20 healthy volunteers formed the control group. Alongside with general clinical trial and the evaluation of their neurologic state, all patients were subjected to the thyroid gland function test by IFA methods, ultrasound investigation and bio-chemical analysis of blood with lipid specter defining.

Among the surveyed patients with hypothyroidism there were 3 men and 17 women, that confirms the data about the greater frequency of the disease among women. The majority of the patients were 45-50 years old. The research included the patients with new-onset primary hypothyroidism and long-term noncompensated ones. The level of free T4 was $6,8\pm2,7$ pmol/l (norm is 10-35), the level of TTG - $17,05\pm2,7$ mcME/ml (norm is 0,3-4,0).

The patients complained of muscle weakness, fatigability and slowness of movements that lead to fall off in working efficiency. In the neurologic state the muscle

strength and tendon reflex reduction came under notice.

The reflex activity of over-segmental parts of the nervous system was studied on the neurophysiological complex «Viking IV M» of the firm Nicolet. The blink reflex was analyzed and registered. A blink reflex is a clinical phenomenon having diagnostic consideration at various forms of neurologic pathology. Contrary to the direct response of the orbicular muscle of eye registered at facial nerve stimulation, the blink reflex is a reflectory response and consists of 2 components: early (R1) and late (R2) ones. The reflex arch of the blink reflex includes the afferents of the trifacial nerve's first ramus, the afferents of the facial nerve, the nidi of these carnial nerves and also the neurons of reticular formation of brainstem. The late response of the blink reflex reflects reflex activity of the brainstem reticular neurons.

The registration of the blink reflex was carried out by means of pickup electrodes, placing them on the orbicular muscle of both eyes. The stimulation was carried out in the output point of the trifacial nerve's first ramus from the one and then from the other sides. Measuring of the silences R1 and R2 was carried out from the stimulus beginning and up to the beginning of the departure from the null line.

The results of the blink reflex research showed that there were authentic parameter changes of its late component (R2). First, lengthening of the latent period occurred, that was $32,2\pm1,7$ msec (P<0,05) on the average; in its turn, this showing was in the range of $27,8\pm0,7$msec in the healthy people. Second, the boundary of the blink reflex induction was $4,3\pm0,5$ mA (P<0,01) in the hypothyroid patients; in its turn, the beginning of the reflectory response registration occurred at the stimulation intensity of $2,8\pm0,5$ mA in the healthy people.

Thus, the carried out research allows assuming that in hypothyroid patients the abirritation of over-segmental structures participating in the realization of brainstem reflectory activity occurs. These changes are associated with the thyroid hormones' deficit which causes the intensification of inhibitory control mechanisms participating in the brainstem reflectory activity realization.

ANTIMICROBIAL EFFECTS OF SODIUM HUMAT FROM PEAT

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The study of antimicrobial effects of sodium humat is considered to be important because the majority of extracted strains of conventionally pathogenic bacteria are resistant to many broad-spectrum antibiotics.

For this purpose the following cultures were used: Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella spp., Citrobacter diversus, Staphylococcus aureus. Cultures were grown on meat peptone agar. The filter disks soaked with 1%, 5% sodium humat solution were placed in a Petri dish with culture and then into a thermostat at 37◦ C. The findings were counted after 24 hours. The experiments showed that the agent had a bacteriological effect.

Rats were used for in vitro experiments. Incised flat wounds were made on their backs to make an experimental model of bacterial infection. One ml of 18-hour cultures grown on Hottinger broth (pH 7,2 - 7,4) with an optic density of 100 mln – 1 mld of colony forming units was placed on the wound. After a 4-day perid, suppurative wounds of the experimental animals were treated with the ointment containing sodium humat at a concentration of 1%, 5% as well as a polyethyleneglycol ointment basis and synthomycin emulsion. After 3-7 days following the wound treatment with sterile tampons, the purulent material was taken and seeded in universal and differential-diagnostic media. Clean cultures were isolated and identified according to their cultural, morphological and biochemical properties.

It has been established that 1%, 5% ointment with sodium humat similar to the synthomycin emulsion has antimicrobial activity as related to Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella spp., Citrobacter diversus, Staphylococcus aureus. The wound surfaces became pus free during a shorter period of time as compared to control animals. The wound

healing was faster in experimental groups in comparison with control rats.

EFFECT LONG-TERM SPACE FLIGHT ON CONTRACNILE PROPERTIES HUMAN SKELETAL MUSCLE

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It is known that inactivity results in deconditioning and physiological deconditioning induced by inactivity affects important system of the body including musculoskelatal. Skeletal muscle deconditioning is associated with adaptation to a microgravity environment. These physiological changes may result in altered muscle function and motor control [Jaweed et al., 1995]. Decrements in motor performance could have negative implications for effective completion of mission-critical operational tasks. Up to now, owing to methodological difficulties, the property contractile properties of human skeletal muscles in a true weightless environment [Tschan et al., 1994; Day et al., 1995] or during its simulation [Grigorieva, Kozlovskaya, 1987; Sugajima et al., 1996] were beyond the field of vision of the scientists who in the main have concentrated on examining the mechanical features of the voluntary muscular contractions. This is the first study to make quantitative measurement of the functional properties of a single muscle in a man exposed to the long-term space mission. The investigation was concerned with the parameters of mechanical responses of the triceps surae muscle, which has been shown to be a postural antigravity muscle [Campbell et al., 1973]. The purpose of study were to analyze the effects of spaceflight the MIR-18 and MIR-22 mission on the mechanical changes of the triceps surae muscle. The methods for measuring electrically evoked and voluntary forces have been described in detail elsewhere [Koryak,

1997]. Briefly, the mechanical responses of the triceps surae muscle were recorded by tendometry, which made it possible to measure single muscle contraction force by the degree of tension change in muscle distal tendon [Koryak, 1995]. Maximal voluntary contraction (MVC), maximal twitch (P_t), tetanic forces (P_o) of isometric contraction elicited by electrical stimulation of tibialis nerve with a supramaximal rectangular pulses of 1 ms at a frequency of 150 Hz [Koryak, 1978], time-to-peak tension (TPT), a half-relaxation (1/2HR), and time of force development both during voluntary and evoked contractions to 25%, 50%, 75% of the MVC and P_o, respectively, before (60-d) and after (6-d) the MIR mission were evaluated as well. The difference between P_o and MVC expressed as a percentage of P_o and referred to as force deficiency has also been calculated. The surface EMG during contractile were recorded a one crewman with bipolar electrodes from the gastrocnemius and soleus muscles. EMG integral (IEMG) was calculated for gastrocnemius and soleus, but were than averaged. The IEMG/MVC ratio was also determined. After spaceflight, the TPT increased by 9%, but 1/2HR and P_t decreased by 18% and 14%., respectively. MVC and P_o decreased by 23% and 11%, respectively. Force deficiency increased by 36%. The value P_o/P_t ratio increased by 6%. The rate of rise a voluntary tension development decreased by 19%, 45%, and 20%, respectively. However, electrical evoked tetanic development not differ substantially from the initial data. The value EMG and IEMF/MVC ratio increased by 55%, and 71%, respectively. These findings indicate thus the alterations of contractile properties induced by spaceflight, were found to be booth of periferal and central nature but more central. However, relative less functional alterations of the triceps surae muscle compared to those observed after a 120-days bed-rest [Koryak, 1995] that may be related to countermeasure compliance.

THE EFFECTS OF LONG-TERM "DRY" IMMERSION ON THE CONTRACTILE AND ELECTRICAL PROPERTIES OF THE HUMAN TRICEPS SURAE

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Various Earth-based models have been used in an effort to simulate unweighting of the neuromuscular system. "Dry" immersion (DI) has been used on occasion to simulate the unweighting effects of spaceflight on human (Shulzhenko et al. (1976) Kosm Biol Aviakosm Med **10**, 82). The results of such studied support the use of Earth-based models. It is known that inactivity results in deconditioning and physiological deconditioning induced by inactivity affects important system of the body including musculoskelatal. Skeletal muscle deconditioning is associated with adaptation to a microgravity environment. These physiological changes may result in altered muscle function and motor control (Koryak (1996) Eur J Appl Physiol **74**, 133, 496). The interesting finding that rhe reduction of the mechanical tension is not proportional to the reduction of muscle weight, fiber diameter, and concentration of contractile proteins (St.-Pierre et al. (1985) Exp Neurol **90**, 635), suggested that electrical activity might contribute to the reduction of the contraction force in disused muscle (Booth (1982) J Appl Physiol **52**, 1113). Up to now, owing to methodological difficulties, the free contractile properties of human skeletal muscles in a true weightless environment or during its simulation were beyond the field of vision of the scientists who in the main have concentrated on examining the mechanical features of the voluntary muscular contractions. This is the first study to make quantitative measurement of the functional properties of a single muscle in a man exposed to the long-term DI. The investigation was concerned with the parameters of mechanical responses of the triceps surae muscle, a postural antigravity muscle (Campbell et al. (1973) Am J Phys Med **52**, 30). The purpose of study were to analyze the effects of 7-day of DI on the mechanical and electrical changes of the triceps surae. The methods for measuring electrically evoked and voluntary forces have been described in detail elsewhere (Koryak (1995) Eur J Appl Physiol **70**, 344). Maximal voluntary contraction (MVC), maximal twitch (P_t), tetanic forces (P_o), time-to-peak tension (TPT), half-relaxation (1/2RT) were measured. The difference between P_o and MVC expressed as a percentage of P_o and referred to as force deficiency has also been calculated. The surface action potential (SAP) was recorded by bipolar surface electrodes applied over the belly of the soleus. After DI, the MVC was reduced by 34% ($p < 0.01$), and the P_o was reduced by 8% ($p > 0.05$). The force deficiency increased by a mean of 44.1% ($p < 0.01$). The decrease in P_o was associated with increased maximal rates of tension development (7%) and of tension relaxation. The TPT was not significantly changed, and 1/2RT and TCT were decreased by 5% and 3%, respectively, but the P_t was not significantly changed and the P_t/P_o ratio was decreased by 9% after DI. The muscle SAP showed an increase in duration (19%) and decreases in amplitude and total area (15% and 3%; $p < 0.05$-0.01, respectively). Comparison of the electrical and mechanical alterations recorded during voluntary contractions, and in contractions evoked by electrical stimulation of the motor nerve, suggests that DI not only modifies the peripheral processes associated with contraction, but also changes central and/or neural command of the contraction. At peripheral sites, it is proposed that the intracellular processes of contraction play a role in the contractile impairment recorded during DI.

NARCODEMOGRAPHICAL PROBLEMS OF PRIAMURYE

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Problem health of submelting generation of representatives aborigenos an Priamurye can not be a speech by only power of organs of public

health. Necessary whole system of state and interstate measures: political, economic, social - for optimization a physician-social help to the child population and conservation of wake Russian society, its strategic power, qualitative reproducing a population. So as a whole, in spite of the general negative trends, narcological situation in Priamurye possible consider controlled. However at the evaluation of general demographic situations in the region were reveal following main factors of shortenning reproduction of population: falls birth rate beside women in the most favorable reproductive ages (25-29 years); negative demographic future is mortgaged in modern age-sexual to the structure a population; increases an average mother age; change reproductive behavior; falls an age threshold of bad habits, including consumption of drugs (from 7-8 years); worsenned condition of surround ambience. In contrast with population census of 1989 year number of population of edge is reduce on 162,3 th.p. (on 10,2%). Specific weight of population of senior able-bodied age in the Priamurye an edge for a period 1989-2002 years is enlarge on 30,2%. Worry causes a correlation of rates of shortenning a number of persons of younger age group in the comparison with growth rates of persons of senior able-bodied age. The number first is reduce on 39,3% (on Russian Far East on 40,9%), but increase on 23,5% (in region on 24,8%). Consequences of such demographic development will negative tell on reproduction functions of population and ensuring an economy of region by the labour in the necessary volume. One of the most important problems of demographic wellfare of Russian Priamurye is a preventive maintenance, early diagnostics and analysis of reasons of spreading is social significant diseases. Our interdisciplinary studies be indicative of presence of close-fitting intercoupling between different ethnics and socio-cultural features, clinical structure, track record variety of psychic frustrations, is criminal-addiction behavior and drug crimes amongst populations of edge on the medical-ecological areas. With such positions is justified all-round consideration of problems of modern population epidemiological analysis, right choice of research priorities, well-marked a realizing an occur change of vectors and directions in the social, medical science and demographic practice.

Development of ethnocultural aspects human population epidemiology carries in itself not only important theoretical stimulus, connected with the crystallization of biosocial paradigm, as well as powerful demographic and sociotherapeutic preventive charge. Supported by The Russian Humanitarian Scientific Fund, grant №06-06-00410a.

PROGNOSTIC METHODS OF ULCEROUS GASTRODUODENAL HEMORRHAGE RELAPSE

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There is a sufficient set of variants of early ulcer hemorrhage relapse (further bleeding) prognostication which is one of the major factors in treatment of UGHR patients. In general, all of them are based on clinical experience, the surgeon's intuition, or on the use of objective endoscopic findings with the application of new complex technologies: endosonography, measuring of mucous coat impedance, redox-potential, etc., which are inconvenient for wide application. There is the authors' opinion, that the recurrent hemorrhage prognostication accuracy based only on endoscopic picture and the blood loss severity has reached the maximum and cannot exceed 70 % (1).

The purpose of our work was to create an analytical system, capable to assist an attending physician in solving tactical questions of UGHR disease management, and based on the bleeding relapse prognostication.

Materials and methods

A retrospective randomized analysis of 411 UGHR case records was carried out by us, the patients having been treated in clinical hospitals of regional centers from 2000 to 2005. A formalized case record (questionnaire of findings) with the unified set of elements, consisting of 125 items was composed. The elements' list (signs, symptoms, laboratory and instrumental data) was being made empirically on the basis of clinical practice. According to the

questionnaire an "Electronic base of UGHR patients for risk factors disclosure in the prognostication of bleeding outcomes" was made. On each sign of the formalized case record its importance concerning the prognostication purpose – bleeding relapse risk, was defined (2.) The significance or reliability of a sign (factor) was defined by means of statistical nonparametric criterion χ^2 (chi-square). The most significant factors on bleeding relapse risk became 84 ones. Among them: the age of 45 years and older, primary hemorrhage episode in a hospital, admission in terms till 5 days, repeated vomiting with blood, black liquid defecations more than 4 times, gastrointestinal hemorrhage in anamnesis, post-surgical hemorrhage, nonsteroidal antiinflamatory drugs intake, organ failure, oedemata, icterus, hemoglobin at the admission less than 70 g/l, ulcer defect size of 8 mm and more, ulcer defect depth more than 5 mm with possible penetration, subcompensated stenosis of duodenal cap with ulcer defect localization in it – the source of bleeding, any protracted bleeding when carrying out an electro-gastroduodenoscopy, the transfused plasma-substituting solutions volume more than 7,3 liters, ignoring eradication therapy, etc.

On the basis of the risk factors importance a computer program was developed: "The program of risk factors search for bleeding dynamics prognostication of patients suffering from ulcer gastroduodenal hemorrhage". The program can be applied in medical establishments of regional and city types, equipped by a minimum of the diagnostic instrumentation and computer technics. Using the patient's checkup results and the disease anamnesis, the results of laboratory and instrumental researches, the obtained data are entered into the program, and after computer processing the doctor receives authentic enough expert opinions on the bleeding relapse risk. Predicting the bleeding relapse threat, the program helps to solve the problem of the necessity to carry out preventive haemostatic actions. It is necessary to recognize, that the conclusions based on the prognostic results, have recommendatory character because the prognostication effectiveness is high enough though, but does not reach a hundred per cent. The responsibility for the treatment outcome is assigned to surgeons; that is why they finally define the choice of medical tactics at UGHR patients.

Conclusions

1. The knowledge of bleeding relapse risk factors allows assuming its probability with sufficient reliability.

2. Program prognostication helps the attending physician to solve the problem of rationality of carrying out emergency preventive haemostatic actions, and aims at the necessity of more skilled experts' consultations.

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ERYTHROCYTES' MORPHOMETRIC ANALYSIS AT THE ELDERLY SUFFERING FROM PANCREATIC DIABETES

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At diabetes (D) it is the erythrocytic component that suffers the reaction of activity increase of free radical oxidation first and is the first to exhaust its compensatory possibilities (E.V. Roytman and co-authors, 2001). However, red blood cells' changes in metabolic disturbance complex associated with D are studied not sufficiently, that is becoming the reason of not always adequate metabolic care (Bondar T.P. and co-authors., 2002). The aim of the research was to study the morphometric characteristics of erythrocytes of the elderly (men and women) suffering from D.

28 persons (15 men of 50,5±3,6 years old and 13 women 56,9±2,5 years old) having suffered from insulin-dependent D of 2 type for 8,6±1,9 and 12,2±2,9 years accordingly, were examined; their hematologic indexes being studied and the erythromorphometry being carried out.

The hematologic indexes of clinically healthy men and women didn't exceed the bounds of the conditional physiological norm. The comparative analysis revealed a higher value of erythrocytes in a blood volume unit by 14, 7%, hemoglobin – by 14, 8%, hematocrit index – by 14, 6% (p<0, 05) at the men. The mean cell value and hemoglobin concentration didn't have authentic differences, but the tendency to higher indexes at the men was marked. Comparing erythromorphometric characteristics of healthy patients we noted that the average diameter (by 6, 3%) and average area of a cell surface (by 5, 8%) were more and the thickness index (by 11, 1%) less at the men; the mean cell volume of red blood cells didn't have authentic differences.

The diabetic patients' red blood indexes were in the bounds of the norm as well, but compared to the control group a more lower value of total and mean cell hemoglobin by 11, 9 and 7, 6, and 17, 8 and 8, 0 % at the men and the women accordingly. The fundamental characteristic of an erythrocyte is volume: at the diabetic patients it was lower - 94,2±0,4 and 84,3±2,34 мкм^3, and 94,3±0,9 and 88,9±2,3 мкм^3 (p<0,01) at the healthy and sick men and women accordingly. In the diabetic patients' groups the diameter-thickness ratio was authentically higher and the specific surface area was lower, the differences being graded more vividly at the women than at the men.

Conclusions:
1) blood of clinically healthy men contains more erythrocytes and hemoglobin in a blood unit volume than that of women, and it has a more higher hematocrit index;
2) sex specificity of the main hematologic indexes retains at the diabetic patients;
3) specific and average surface areas and the average volume of an erythrocyte is lower , but diameter-thickness ratio is higher at the patients;
4) geometric profile changes of red blood cells decreases their contribution in normal functioning of homeostatic systems of a body at diabetes;
5) hematologic profile and morphometric characteristics' changes of erythrocytes at diabetic patients are valued as adaptive processes aimed at blood flow properties perfecting and reducing tissue hypoxia in erythron system.

ESTIMATION OF X-RAY INFLUENCE ON SPINAL GANGLIA NEURONS

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Practically all the population of all countries in the world is exposed to X-ray effect when being diagnosed or taking remedial measures during the life. In this respect there is a necessity to study the changes, including biochemical parameters, taking place in sensory neurons of spinal ganglia when X-rayed.

The research was carried out on 81 mature guinea-pig males, from which 51 were used in the experiment, and 30 served as the control. The experimental animals were exposed to single general irradiation (dosage – 5 Gy, filter – 0,5 mm SI, voltage – 180 kV, amperage – 10 mA, focal distance – 40 cm). Excluding the animals from the experiment and sampling the materials were done immediately, in 6 hours, on the 1st, 5th, 10th, 25th and 60th days after finishing the exposure. Spinal ganglia were taken from different parts of spinal cord (cervical, thoracic, and lumbar). The LDH activity level in the cytoplasm of sensory neurons of spinal ganglia was subjected to the histoenzymologic research. The findings were statistically treated.

Immediately after finishing X-raying the increase of the LDH activity level in the spinal ganglia neurons of all parts of the spinal cord was marked; it being: 110,5% in the cervical part, 123,9% in the thoracic part, 109,4% in the lumbar part of the spinal cord, from the basal value (P<0,05). In the following periods the LDH activity keeps retaining increased being, in

particular, 128,8% in the spinal ganglia of the cervical part, 107,8% - of the thoracic part and 104,6% - of the lumbar part of the spinal cord, from the control value (P<0,05) on the 5th day. By the end of the observation period (60th day) the retaining of increased LDH activity level is marked, being 154,1% in the neurons of the cervical part, 143,8% - in the thoracic part and 122,3% - in the lumbar part of the spinal cord, from the basal value (P<0,05), that testifies a significant change of LDH activity in the specified cells when being exposed to X-rays.

INFLUENCE OF MICROVAWES ON EPIDERMAL SKIN CELLS

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During the last years in everyday life and industry as well as while taking diagnostic remedial measures, sources of SHF radiation (microwaves) get more and more popularity. In this respect the necessity to study biochemical changes in epidermal skin cells, including basaliocytes, while being affected with microwaves, develops.

The research was carried out on 65 mature guinea-pig males. The animals were exposed to the effect of microwaves of thermal intensity (length of wave - 12,6 cm, power flow density (PFD) – 60 mW/cm2, exposure time – 10 min). The exposure happened at one and the same time – from 10 to 11 a.m.. Excluding the animals from the experiment and sampling the materials were done immediately, in 6 hours, on the 1st, 5th, 10th, 25th and 60th days after finishing the effect of the specified factor. The flaps of skin were taken from different areas (head (cheek), back, stomach). The succinate dehydrogenase (SDG) and nicotinamide adenine dinucleotide 2 (NADN2) activities in the cytoplasm of the epidermal basal layer were subjected to the histoenzymologic research. The findings were statistically treated with the use of Student criterion.

Immediately after the microwave exposure the SDG and NADN2 activity decrease is marked, being: in the skin of head - 92,3% (98,0%), back - 90,8% (95,5%), stomach - 88,3% (97,7%), from the basal value accordingly (P<0,05). Later on the SDG and NADN2 activities keep on decreasing, achieving the minimum on the 5th day. Thus, in particular, the SDG activity on the defined term is: in the skin of head - 90,0%, back - 86,4%, stomach - 78,2% (P<0,05). In the following periods the SDG and NADN2 activities in basaliocytes increase, reaching the initial showings in most of the flaps on the 60th day, the SDG activity level in basal skin cells of back and stomach being 97,3% and 95,1% from the control level accordingly (P<0,05). The findings received testify significant changes of the SDG and NADN2 activities in the cytoplasm of the epidermal basal skin cells when being exposed to microwaves.

SIGNIFICANCE OF THE β -2-ADRENERGIC RECEPTOR (β-2AR) POLYMORPHISM IN ASTHMA AND ATOPY

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Last years many researchers specify growth of allergic diseases, resistant to traditional methods of therapy. From the earliest stages of occurrence of the doctrine about an allergy allergic reaction consider as reaction of an inflammation. Complexity of process will be, that attributes of an inflammation are reflection of a mobile combination of effects of the various cells which are taking place in a different functional condition, different intermediaries (mediators), having different concentration and diffusion characteristics. Atopy is wide and multiplane pathological process. The estimation of this pathological process from positions of the general pathology means the analysis of the reasons and the general laws of development atopy. Discussion at a modern level of the theory

about decrease β-adrenergic reactance, as is meaningful to basis of development atopic diseases.

At atopic diseases decrease β-adrenergic reactance comes to light. It is shown by a smaller degree glikogenolis, lipolis, increases arterial pressure and educations cAMPH in leukocytes at addition of adrenaline. There is growing evidence, that asthma and atop are genetically linked, although the genetic control of both diseases may be present at several levels sensitization and specific IgE responses, mediator release, end organ responsiveness or phenotype expression. It is assumed, that asthma may be a result of primary defect of β-2AR function, that an impaired β-adrenergic function may be also related to IgE responsiveness and atopy.

New exciting data are related to the recently found polymorphism of the β-2AR. The gene for the β-2AR, which is localized close to the IL-4 gene duster on chromosome Sq, has been previously cloned, and sequenced. It is established that several point mutations exist within the gene coding region, resulting in changes in the amino acids sequence. It is shown, that the changes in the aminoacid sequence of the extracellular aminoterminus of the receptor affected the function of the receptor. For example, the presence of glycine at position 16 (Glyl6) was associated with enhanced regulation of the receptor in the response to agonist as compared to arginine at this position (Arg16), and substitution of Glu for Gln at position 27 resulted in a decreased regulation of the receptor. It is assumed, that this polymorphism may affect bronchial smooth muscle function in vivo. In fact, study of the Gln/Glu 27 polymorphism, and airway hyperreactivity in a group of patients with mild to moderate asthma revealed that Gln27 homozygotes had a four-fold higher bronchial hyperresponsive-ness to methacholine (lower threshold dose), than patients who were homozygous for the Glu27 form of the receptor; heterozygotes had an intermediate hyperreactivity. Population study, demonstrated similar frequency of Gly/Arg16 and Glu/Gln27 polymorphism in asthmatic and normal subjects. It is indicating, that polymorphism is not a major cause of asthma. However, comparison of the frequency of the β-2AR genetic variants in patients with nocturnal and non-nocturnal asthma reveled, that the Gly 16 allele was significantly more frequent in the nocturnal group as compared to the non-nocturnal group.

These data indicate, that β-2AR polymorphism may be closely related to the asthmatic phenotype, and severity of the disease. Since β-2AR are present on immune cells like lymphocytes, macrophages and granulocytes, being involved in modulation of inflammatory mediators and cytokines release, it has been postulated that, genetic polymorphism of β-2AR may also be associated with the expression of the atopic phenotype.

THE USE OF INTERFERONS IN CHRONIC VIRAL LIVER DISEASES
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The increased disease a chronic hepatitis and low efficiency of treatment causes necessity of profound their studying immunopathogenesis and development of new methods of therapy. The broad effects of intercellular actions of interferons (IFN) can be roughly divided into: a) antiviral, b) anticancer, c) immunomodulatory. IFN are not produced constantly, so that their concentration in normal tissues is minimal or undetectable. However, after stimulating factors, esp. infections, their level in tissues highly increases, as a result of the activation of immunocompetent cells; later IFN bind to their specific receptors.

The strongest antiviral action exerts IFN-α. It influences all the stages of viral replication, but most important is inhibition of the genome translation, what makes defective the synthesis of viral proteins (kinases phosphorylate). The second mechanism of translation inhibition is the

induction of 2'5'-oligosynthetase which degrades viral RNA. Both mechanisms omit healthy cells in their inhibitory actions. Furthermore, antiviral effect is achieved also by the increased expression of histocompatibility antigens and stimulation of the immune response. Interferons are now produced in the recombinant form, what enhanced their broader use. They are offered for treatment of adult patients and children with a chronic hepatitis. However, IFN-α is most widely used for the treatment of chronic viral hepatitis B and C.

We report results of treatment of 184 children, mostly with chronic aggressive type B hepatitis, HBsAg and HBeAg positive. Treatment consisted of 3 weekly, doses of 3 MU recombinant IFN-a, mean: 4.51 MU/m2 for 16 weeks (ca. 3 months). In the evaluation one year post IFN: 12% of children proved to be complete responders [HBsAg(-), eAg(-)], 53% of children partial responders [HBsAg(+), but eAg(-)], and 35% - nonresponders [HBsAg(+), eAg(+)]. The treatment was quite well tolerated; but such side effects as fever, loss of appetite, headaches, muscle and joint aches were noted in over 10% of children. The reference (unrelated) group consisted of 77 children (53 boys and 24 girls). During the same period, 2.6% of them became complete responders, 22.1% - partial responders and 75.3% remained nonresponders.

Moreover, in part of the treated children (n-23) we have determined pretreatment prognostic factors, by measuring HBeAg, HBsAg and HBV-DNA quantitatively, in addition to ALT and clinical chemistry. We have found differences between arithmetic means of these parameters, but because of big range of results, the statistically significant differences were obtained only in relation to age of children and HBeAg concentrations. We have shown, that low initial level of HBeAg, HBsAg, low level of HBV-DNA, as well as relatively high ALT value, together with rather low age of children were connected with the good prognosis for response. With regard to chronic hepatitis C - female gender, lower level of HVC-RNA, and lower age, but elevated baseline ALT were associated with good prognosis for response to INF-α therapy.

However, monotherapy with INF-α would give sustained response (persistent normalization of transaminases and negative HCV-RNA) in only ca. 20% of patients after 2 years of follow-up. In adults, interferon combined with ribavirin may raise the effectiveness about 2 times. Our current project in children concentrates on the inhibition of metabolites of arachidonic acid formed during the INF therapy. These metabolites, including prostaglandins (PGE2) and tromboxanes could be suppressed by inhibiting cycloxygenase with indomethacin.

MAJOR FACTORS, INFLUENCING QUALITY OF LIFE IN RUSSIAN PATIENTS WITH DIABETIC FOOT SYNDROME

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Quality of life (QoL) as one of the basic criteria of treatment efficiency, received worldwide circulation in last years. Many authors (Dedov I., 1998; Ashford R., 2000) mark, that the purpose of therapy of chronic diseases is not in treatment itself, but in improvement of patient's life as a result of severity decreasing or restriction of illness progressing.

The augmentation of life expectancy in patients with diabetes results in annual increase of late complications, one of which is the diabetic foot syndrome (DFS) – the condition, combining neuropathic and vascular disorders of the lower extremities. It conducts to occurrence of foot ulcers and other severe complications, such as diabetic gangrene. DFS is recorded in 30-80 % patients with diabetes (Reiber G., 2001).

However, there is a paucity of research into the specific effects of foot ulceration on the QoL of patients (Ashford R., 2000). Further, although studies have reported psychosocial concerns experienced by patients with diabetes and the complications of lower extremity ulcers, there is little qualitative research which outlines patients' perspectives of living with foot ulceration.

The purpose of our work was researching the major factors influencing quality of life in patients with DFS. Research was carried out on the base of Chelyabinsk Diabetes Center, which contains podiatry department. 145 patients with diabetes type II in the age from 40 till 70 years were included in survey. According to the program we have generated two groups: study group of 100 patients with of neuropathic DFS (DFS group) and control group of 45 persons with the risk of purulent DFS complications.

Measuring of QoL in patients with DFS is not a simple task. General measures such as the SF-36 are extremely useful for comparisons of function across diseases, but they do not capture specific problems posed by diabetic peripheral neuropathy and are less useful for framing clinical interventions (Vileikyte L et al., 2003). So the study was carried out with MOS SF-36 modified questionnaire which contained the set of special questions for the given pathology. To a standard SF-36 questionnaire we added 13 items, concerning specific reaction of the patient on problems, connected with DFS. The questionnaire has been tested in earlier pilot research.

Measurement of QoL parameters was performed at outpatient reception in Diabetes Center and in surgical infections department of Chelyabinsk City Hospital.

According to SF-36, in DFS group the majority of QoL parameters appeared significantly lower than in control group. Estimation of physical fitness (PH) was 31,8 points versus 42,5 (decrease on 25%, $p<0.05$), role physical (RP) – 28,7 versus 41.2 (decrease on 30%, $p<0.05$), bodily pain (BP) – 30,8 versus 44,5 (decrease on 31%, $p<0.05$), general health (GH) – 33,3 versus 35,8 (decrease on 8%, $p>0.05$), vitality (VT) – 38,5 versus 46,9 (decrease on 18%, $p>0.05$), social functioning (SF) – 39,5 versus 44,6 (decrease on 12%, $p>0.05$), role emotional activity (RE) – 32,3 versus 40,5 (decrease on 20%, $p<0.05$), mental health (MH) – 34,2 versus 40,4 (decrease on 15%, $p>0.05$). The same tendency goes to such integral scales as physical component summary (PCS) – 31,2 versus 42,3 (decrease on 26%, $p<0.05$) and mental component summary (MCS) – 38.0 versus 42,6 (decrease on 11%, $p>0.05$).

In that way, values of all QoL parameters, except for GH, VT and SF are significantly lower ($p<0.05$) in DFS group. The greatest problems in patients with DFS were associated with bodily pain and restriction physical activity

According to WHO recommendations, criteria of QoL should be studied in five directions - physical, psychological, adaptive, social and environmental factors. In each specified sphere we have revealed the major factors influencing on QoL and their comparative weight in researched groups. Due to self-estimation of patients in the physical sphere greatest weight has such factor, as foot care skills – 19% in DFS group versus 10% in control group. In the psychological sphere of life greatest weight has such factor, as mode of life changing – 19% versus 35%, in social and adaptive spheres of life the main factor is welfare - 43% versus 20%, and among the environmental factors patients value the support from their family and community - 33% in DFS group versus 50% in control group.

From the submitted material follows, that the level of knowledge and possession of a foot care skills is considered more important in group of DFS complications. At the same time patients with DFS suffer from restrictions of a habitual way of life more and attach to this the greater value. We have noted, that restriction of well-being in group of risk is more expressed, than at patients with DFS. The most authentic explanation is presence at patients with DFS not only moral, but also material support from family and society. Also research has shown, that patients with DFS are better adapted to a changed condition, both in psychological, and in the social plan. This implies, that DFS patients appreciate support of the family, community and the state, they own more effective forms of interaction with any structures, whence can receive the help.

Thus, we count, that QoL estimation should be included into standards of help to the patients with DFS and may be in the competence of specialized nurses.

THE METHOD OF DETERMINING THE FUNCTIONAL CONDITION OF ERYTHROPOESIS IN FROGS

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The morphology of a cellular surface is individual for each type of cell and undergoes essential changes during various phases of the cellular cycle, the transformation of cells, influences of various chemical agents. At the same time, various endocellular processes are morphologically reflected on the cellular surface that is one of the fundamental positions of evolutionary physiology about connecting the processes of form with the function of the cell. The purpose of this research is the study of cellular-system mechanisms which regulate the membrane of the homeostasis and the function of the erythrocyte line hemopoesis in frogs.

Peripheral blood of Rana ridibunda frogs served as material for research. The mechanisms of membrane regulation of cellular geometry were investigated according to the methodology developed by us (patent of the Russian Federation № 22268463 «Ways of estimating the activity of erythropoesis»). From each sample (the sample was incubated into 0,2 % a solution of sodium chloride) and control (control was incubated into 0,65 % a solution of sodium chloride, in the ratio blood/incubatory environment 1:50 within an hour) a single-layered suspension for preparations was prepared. From the preparations images with the «Videotest» system were registered every 30 sec for 10 minutes and then in addition every 10 minutes during an hour. The dimensions of all nuclear erythrocyte were measured. The biometric indices of cells were counted based on the given parameters and the erythrocyte population were classified as two functional groups: recytus and letaliocytus. An estimation of erythropoesis activity was carried out at a value time interval during which there was a transition of the greater part of cells to the letaliocytus class, which coincided with the starting point of incubation.

The results of our research established, that it takes 30 sec for the incubation samples to reach the correlation of 8:22 of the letaliocytus to the recytus, Accordingly, in 60 sec of incubation the quantity of recytus decreased, but the correlation reached 8:14, and within 150 sec of incubation - 14:9. Thus, the system of hemopoesis was in a state of activating the erythropoesis. A growing percentage of the letaliocytus over the recytus was observed on the 150-th second concerning the equilibrium condition (from 30 sec up to 60 sec). The circulation of functionally young cells having a sufficient membrane potential point out to the activation of erythropoesis. The percentage of the letaliocytus and the recytus during each time interval will be in straight dependence on the metabolic potential of the process of erythropoesis as a whole, defining the biochemical maturity of the cell.

MORPHOLOGICAL ALTERATIONS IN THE LUNGS DURING WEST NILE VIRUS INFECTION

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West Nile virus (WNV) is an enveloped, neurotropic, single stranded (+) sense RNA flavivirus, first isolated from a woman in Uganda in 1937 (Smithburn K.C. et al., 1940). Since then it has reemerged multiple times: first in Europe, Asia and most recently during the 1999 in the Volgograd Region of Russia and in the United States (Hubalek Z., Halouzka J., 1999; Lanciotti R.S. et al., 1999; Pisarev V.B. et al., 2000). The virus, which has spread rapidly throughout Volgograd Region, may cause severe illness especially in the elderly (manifested by meningitis and encephalitis) that may lead to paralysis, coma, and death. During the 1999–2002 outbreaks of WNV in the Volgograd Region, more 1,000 cases were reported, including 18 deaths (~1.8%) (Lvov D.K. et al., 2004). Central nervous system (CNS) expression of the chemokine receptor CCR5 and its ligand CCL5 was prominently up-regulated by WNV,

and this was associated with CNS infiltration of CD4+ and CD8+ T cells, NK1.1+ cells and macrophages expressing the receptor. It is considered CCR5 is a critical antiviral and survival determinant in WNV infection of mice that acts by regulating trafficking of leukocytes to the infected brain (Glass W.G. et al., 2005).

In the Volgograd Region 23.6% cases of West Nile fever during the 1999–2002 without meningitis and encephalitis were reported (Petrov V.A., 2004). WNV infection leads to morphological alterations in different organs. Postmortal examination has found mononuclear aggregations in bronchial walls, perivascular mononuclear infiltration, pulmonary edema and focal hemorrhages, but clinical alterations of respiratory functions were not detected (Grigoryeva N.V., 2005). The morphological pathogenesis of pulmonary WNV infection is poorly understood.

Here, we characterize a mouse model for WNV infection using a intraperitoneal route of infection. White mice were infected i.p. with 10^3 focus-forming units (ffu) of strain WNV Astr 986, identical to WNV-NY99, which imitates the natural route of WNV infection in man. Mortality was 20% at that dose. The grope of surviving mice constitutes 8 animals. Lungs obtained from mice at day 9 after induction of WNV infection were fixed in 10% (weight/volume) neutral buffered formalin, were embedded in paraffin and were cut into sections 5 µm in thickness. Sections were stained with hematoxylin and eosin for routine histological analysis.

In pulmonary bronchi mononuclear aggregations in bronchial walls were found. They occupied all layers, but the most prominent density of small lymphocytes was in the adventitia. Lymphoid infiltration spreads on the surrounding tissues and was more prominent around small blood vessels. Hemodynamic changes were also found: hyperemia, stasis in capillaries, perivascular hemorrhages. Interalveolar septa were edematous, infiltrated by small lymphocytes and macrophages. Alveolocytes were edematous, some of them desquamated. Inside alveoli serous liquid was found, but in some cases hemorrhagic infarctions were detected.

Intrapulmonary autonomic ganglia contained polygonal neurons with vacuolated cytoplasm of perikarya. They nuclei were rounded vesicular with one or two ectopic nucleoli. Part of neurons had hyperchromic cytoplasm of perikarya. Satellite neuroglial cells were with minimal dystrophic alterations. Lymphoid infiltration and interstitial edema of ganglionar capsule and stroma were found.

Our findings suggest that endothelial cells in the lungs of WNV infected mice regulate migration of leukocytes to the infected lung. The damage of peripheral nervous system participates in pathogenesis WNV infection. The data also raise important new questions about the potential roles of regulatory systems that are induced by WNV in this model and in man.

DEMONSTRATION FEATURES OF SOMATIC MOTHERS' DISEASES WHO HAVE DAUGHTERS WITH BROKEN MENSTRUAL FUNCTIONS

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Children's health is determined by somatic health of their mothers at the expense of both spontaneous communicate of genetic material and inside uterine (antenatalis) damages because of complicated flowing of pregnancy and childbirth. Infringement in the making of young girl's menstruation is the first clinic display of dysfunction of reproductive of reproductive system as a reflection of justifiability of their somatic health.

The aim of our work was lighting of demonstration peculiarity of mothers' somatic diseases who have daughters with broken menstrual function in pubescence (pubertatis) period.

Anamnesis and clinic characteristics of 232 women who have daughters at the age of 15-18 with gynaecological age duration more than 2 years were valued. The main group was 116 women who have daughters with broken menstrual function. Another

group of 116 women for comparison has daughters with physiological flowing of pubescence period.

The age of first menstruation and a character of the beginning of the women's menstrual function in the comparative groups aren't greatly different.

Real difference in the clinic demonstration of diseases of ears, noses, threats organs 57(49,1%) the daughters have their broken menstrual function and 14(12,1%) cases with of it, renals 24(20,7%) in the main mothers' groups and 5(4,3%) in the comparative group was revealed.

Somatic mothers' diseases serve not only as negative background for bearing their daughters with following problems in their beginning of the reproduction, but their early menses testifies to considerable lowering of general organism adaptive possibilities.

Diseases of endocrine (glands) 77(66,4%) and 31(26,7%), heart-vascular ones (59(50,9%) and 38(32,8%), ears, noses and throats 38(32,8%) and 15(12,9%), alimentary canal ones 39(33,6%) and 16(13,8%) as well were lighted among the mothers who have daughters with broken menstrual function after their mother's birthing and before the age of 40 (reproductive period) really oftener than among mothers who have daughters without such diseases.

Frequency of exposing of somatic diseases didn't have authentic differences among women after 40 in the comparative groups. Although heavy climacteric syndrome 12(10,3%) and malignant tumours of a reproductive in the main women's group after 40.

Thus presence of their mother's somatic diseases in their pregnant and their authenticity earlier clinic demonstration in their reproductive age influences on the reproductive girl's health negatively as the lowering display of their general adapted organism abilities.

IMMUNE STATUS OF HORSES AT CHRONIC STRONGYLOIDOSIS

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Strongyloidosis of horses refers to the class of helminthiases, which are caused by parasitizing intestinal worms Nematode of the superfamily Rhabditoidea, genus Strongyloides, species Strongyloidides westeri.

The disease's agents parasitize in the small bowel, and though they are little pathogenic, under certain circumstances they can cause a nasty enteritis.

Strongyloidosis represents a unique genus: helmints are able both to parasitize in an animal's body and to be free to propagate out of an organism. Only ambosexous females, which strike their eggs containing larvae by parthenogenesis (i.e. the development occurs from infertile egg cells), parasitize in the small bowel. After getting rid of the eggshells the larvae go through 4 phases developing into free-living males and females, and then helmints can propagate in the ambient medium.

The vermination can occur when ingesting - alimentarily, or through skin – percutaneously,

free-living 3rd stage larvae, which then migrate through low tension circulation, lungs, breathing tube to the small bowel, where they develop into full-grown females.

Though there are lots of reasons for the helminthism to appear and they are all interconnected, one of the most important ones is the immune status change of animals, as it is stated that animals become more responsive to helminthisms at the immunity weakening (G.M. Urkkhart and co-authors, 2000).

That is why the aim of our work is to define the immune status of horses at chronic strongyloidosis on the basis of studying of the value of humoral immunity indexes in blood serum.

The research was carried out in the cavalry school "Squadron", Sovetsky, Khanty-Mansi Autonomous Area, Tumen Region. In the

experiment horses aged 3 years were used, two experimental groups being formed. The first group was the control one and consisted of clinically healthy animals. The second group was an experimental one, there were horses that were diagnosed to suffer from chronic srongyloidosis on the basis of clinical signs (parasitic enteritis) and the results of scatology by Fuelleborn-and-Berman-Orlov method, the occurrence of eggs and larvae of helmints in the fecal masses being proved.

The material of the research was fasting blood taken from the jugular vein in the morning and motionless. In the blood serum the value of immunoglobulins of A-, M-, and G-classes was defined by the single radial immune-diffusion method with the use of monospecific antiserums, the concentration of circulating immune complexes (CIC) - by the spectrophotometric method, blood serum lysozyme activity - on the selective lytic lysozyme activity concerning the sensitive culture Micrococus lisodercticus, the bacterial growth-inhibitory activity - according the method of Smirnova O.V. (1996) were measured. The research results are shown in the table.

The host immunity limits the contamination level changing the development of new invasions or stopping their development completely or on larval phase, while the existing invasion with full-grown helmints either is extruded or their egg producing decreases considerably (G.M. Urkkhart and co-authors, 2000).

As it is seen from the tables 1 and 2, chronic invasion is accompanied with dyscrasia of humoral component of immune system. It is the after-effect of helmints' allergenic influence on the host's body and the interaction result of the system "antigen-antibody", helmints themselves and larvae migrants and their waste products playing the role of antigens.

Table 1. The immunoglobulin value in the horses' blood serum, n=10 (Sx±x), * - P ≤ 0,001

Animal groups	Immunoglobulin classes, g/l		
	Ig G	Ig M	Ig A
Control	16,51±0,53	2,29±0,11	1,86±0,06
Experimental	22,30±0,65*	2,39±0,13	1,03±0,10*

The analysis of the results of the study of immunoglobulin value in blood serum of the horses at chronic invasion showed that the quantity of IgG increases by 34-37%.

70-80% of the total immunoglobulin value in blood serum is allotted on IgG. They play the main and foundational role in humoral immunity at antigenic loading causing the pathogenic agent's death with a compliment factor and opsoning the phagocytal cells; are able to neutralize bacterial exotoxins, to bind compliment and to react precipitation.

IgG increasing testifies the adaptive humoral immune reaction of a body to the helminthism invasion and is connected with the influence of nematodes' antigens, their waste products, their self-tissue and the following-up bacterial population destruction. The IgG level increase may also be associated with the fact that the mucus membrane with hyperpermeability allows anthelmintic immunoglobulin G to "go out" of plasma into bowel lumen and to have an access to parasites.

We haven't established authentic IgM level change at chronic horse strongyloidosis. It is known that immunoglobulins of the class M are "the earliest" of all immunoglobulin classes. They are able to agglutinate bacteria, neutralize viruses, activate compliment.

The data got by us testify a greater probability that IgM-antibodies don't participate in chronic invasion pathogenesis.

We have established that chronic srongyloidosis of horses is accompanied with an authentic decrease of the IgA level by 40-45%.

Immunoglobulin A is a secretory immunoglobulin. It refers to the main immunoglobulin class which is concerned with local immunity, prevents bacteria from attaching to the mucus membrane, neutralizes enterotoxins, activates phagocytosis and compliment. The IgA concentration decrease allows assuming the existence of suppressive mechanisms at chronic invasion, which can underlie the synthesis inhibition of immunoglobulins of the given class.

Besides, it has been established that in the acute period of nematodosis of gastrointestinal tract at heavy beasts and sheep the adaptive immunity to helminthisms is formed. The immune response is a complex one, and is based on the antigenic stimulation with secretory or excretory products egested during the development of a 3rd stage larva into a full-grown species. For example, the experimental research showed that mature sheep possessing the immunity to Ostertagia can ingest up to 50000 3rd stage larvae daily without any clinical signs of parasitic gastritis. There are also the data that the secretion of anthelmintic immunoglobulin A on the mucus membrane surface promotes the functional blennogenous cell's activity increase.

Therefore, the IgA concentration breakdown promotes (at reinvasion of horses with nematodes' larvae) larvae's migration, their development into full-grown species, their fertility increase and, as the consequence, helmints' disease-evoking power's increase. It leads to the fact that helminthism occurs with pronounced clinical signs.

We have established that the horse body responds to the entry of nonshared antigens with the synthesis of proteins possessing specific affinity to the antigen which causes this synthesis. This conditions the appearing in the blood circulating immune complexes (CIC), the concentration of which is one of the criteria of functional competence of the humoral component of the immune system of animals (Isayev A.G., 2001). The CIC level at chronic invasion increases more than by 30%, that can be the consequence of non-sufficient rate of utilization by the elimination of the given complexes against the background of the increased antigenic loading to a body.

Table 2. The humoral immunity indexes, n=10 (Sx±x), * - P ≤ 0,05; ** - P ≤ 0,01

Indexes	Control group	Experimental group
Circulating immune complexes, %	25,85±0,66	31,15±1,63*
Blood serum bactericidal activity, %	66,88±2,47	80,09±2,57**
Blood serum lysozyme activity, %	27,37±1,23	34,50+0,84**

One of humoral resistance factors is the lysozyme enzyme, the place of synthesis of which macrophages , from where it enters blood and then leucocytes (granulocytes), serve. The biological meaning of lysozyme is founded on its antibacterial properties. In our research we have established the authentic increase of lysozyme and bactericidal blood serum activity, that testifies the state tension of natural defensive mechanisms of horses and their and agent interplay level, i.e. the stimulation of the phagocytosis process during chronic invasion.

So, we have established that the immune status of horses at chronic strongyloidosis is characterized by IgG level increase and IgA concentration decrease. The specific redistribution of main immunoglobulin classes in blood serum of animals, probably, creates favorable conditions for larvae's migration in the host body after the vermination, the development of the 3rd stage larvae into a full-grown species, nobilous female fertility increase and their disease evoking power increase. That is why chronic invasion occurs with pronounced clinical signs in the image of parasitic enteritis. Alongside with local disorders conditioned by helmints parasitizing in animals' bowels the CIC concentration, bactericidal and lysozyme activity increase occur. It means that nobilous helmints, larvae migrants, their waste products and secretory and excretory products egested during the development of a 3rd stage larva into a full-grown species appear as antigenic stimulator for a horse body.

The data got allow us to make the conclusion that helminthic invasion is not a separately taken pathology, but represents a difficult system complex appearing as the result of host body affect with helmints and is accompanied with animals' immune status changes. That is why it is necessary to include the preparations decreasing the sensibilizing action of helminthic invasion on the host body and increasing the synthesis of immunoglobulin of class A into helminthism treatment schemes additionally alongside with anthelmintic agents.

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GENERAL ADAPTATION REACTION OF ERYTHROCYTIC BLOOD POPULATION OF BIRDS AT PHOTODESYNCHRONOSE
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The erythrocytic membrane penetration (EMP) and sorption capacity (ESC) are the objective characteristics for the estimation of structural and functional state of the membrane apparatus of a body as a whole, considering a high correlation of property changes of blood cells' membranes and internals at extreme exposures of different intensity. The aim of the research is to study birds' EMP and ESC states when adapting to photodesynchronose.

The work was carried out on 15 cockerels of "Isa Brown" cross. Photodesynchronose was created by a photo-modeling method according to 3-days inversion of light exposure in the light status of photoperiod 12:12 (from 8 a.m. till 8 p.m. – a night imitation, from 8 p.m. till 8 a.m. – a day imitation) with the following birds' change-over on natural light status. The blood was taken on 1,3,7,15,23 and 29th day after chronophysiological loading. EMP was evaluated on the urea intensity to penetrate through cell membranes; ESC – on membrane sorption of methylene blue;

plasmatic (ectoglobular) hemoglobin (PH), blood glucose level, osmotic fragility and acid fastness of erythrocytes – by means of traditional in clinical and veterinarian hematology methods.

In the background survey the average percentage of erythrolysis (APE) and the average percentage of hemolysis in the area of urea concentration 55:45 and 60:40 were accordingly $4,06\pm1,68$ and $4,10\pm2,39$. On the first and third days of rehabilitation period EMP was highly increased – APE was 4,9 and 6,5 fold higher the control level accordingly. Simultaneous ESC decrease we consider as a tendency. The PE increase – up to $1,99\pm0,35$ and $1,26\pm0,19$ g/l^{-1} (in the control $0,68\pm0,13$ g/l^{-1}, $p<0.01$) – witnesses the damageability of membraness. Hemoglobin breakdown products, being a powerful prooxidant, initiate lipid peroxidation (LPO) and, causing membrane ruptures, provoke EMP increase. Erythrocytic membrane structures' destabilization leads to their functional inadequacy and hypoxia. The glucose concentration in blood decreases up to $7,40\pm0,15$ and $6,88\pm0,08$ $mmol/l^{-1}$ ($p<0,001$). On the seventh day a hyperglycemic rising ($9,88\pm0,28$ $mmol/l^{-1}$) is marked, EMP and PE are higher the control level, and the sorption capacity is lower by $17,5$ % ($p<0,01$). In two weeks the glucose concentration in blood is $11,27\pm0,47$ $mmol/l^{-1}$ and the APE and PE tend to decrease; on the 23, 29 days the studied parameters approach the background ones. The evolution of regenerative processes in erythrocytic population is reflected in the differential acid erythrograms. On the first week of the stress aftereffect the functional erythron activity increases, the population of old cells with decreased resistance grows, and a specific shift of red cell distribution resistance erythrogram to the left is marked, that witnesses the resistance decrease and erythrolysis intensification. The right wing rising and the hemolysis time increase up to 6 min on the 15 day of the adaptation period – is the sign of the population's rejuvenation. On the 23 day the right shifted erythrogram becomes tricrotic and stretched to 8-9 min; on the 29 day the acid resistance increases, the erythrogram profile approaches the background one, however, in the erythrocytic population the lot of cells with hidden structural membrane failures is still high – up to 84,7 % red cells hemolyzes in the critical resistance point (0,55 % NaCl) and up to 21,0 % - in the autohemolysis point (0,70 % NaCl). The stressor reaction and the

associated with it hypoxia are fraught with metabolic disorder and endogenic intoxication of a body. At metabolites' over accumulation in blood plasma the toxic loading on cells' membranes increases, their receptors are blocked, and the sorption capacity decreases.

So, phtodesynchronose provokes at birds the development of general adaptive syndrome of erythrocytic population manifested with EMP, PE increase and ESC decrease.

Shot report

BIOLOGICAL ASPECTS OF INFRINGEMENTS THROMBOCYTE HEMOSTASIS

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The research of trombocytic infringements at newborn calves with dyspepsia has the important practical meaning, because the activation of a primary link hemostasis plays a conducting role in activization hemostasis as a whole, increase of viscosity and deterioration hemorheology with inclination to itravascular thrombocytes formation. At the same time the infringements aggregative of ability thrombocytes and its itravascular of activity are very poorly investigated. The purpose of work is to research features of infringement trombocytic of a link hemostasis at newborn calves with dyspepsia.

Materials and methods

75 newborn calves with dyspepsia for 1-3 days from 1-2 calving the healthy cows were under supervision. The feeding and the contents was carried out in standard conditions of calf-house. 24 healthy newborn calf have compounded of control group. The capture of blood was conducted at morning o'clock. The inspection included definition of level average molecules in plasma and washed and resuspendition thrombocytes on [1]. Activity of peroxide oxidation of plasma lipids (POL) was defined under the contents of TBA-active products, acylhydroperoxides (AGP) [2], and intrathrombocyte the POL on concentration of a basal level of malonic dial in reaction of restoration by an thiobarbituricum acid [12], in updating [7] and AGP [2]. Intrathrombocyte antioxidation system characterized activity catalase and superoxiddismutaza (SOD) [8].

In resuspendition thrombocytes was defined the contents of a cholesterin by an enzymatic colorimetric method, and phospholipids on phosphorum [6]. Activity and time of formation endogenic thromboplastin was investigated [10]. Indirect estimation of arachidonic acid metabolizm in thrombocytes was defined by T.A Ermolaeva's and co-authors (1992) method with registration at photoelectriccolorimeter [5]. Calculation of quantity thrombocytes in capillary blood made in the Goryaev's chamber. Aggregation of thrombocytes (AT) was investigated by a visual micromethod [3] with ADP inductors (0.5×10^{-4}M.), collagen (cultivation 1:2 of the basic slurry), thrombinum (0,125u.e./ml.), ristomycinum (0,8 mg/mls.), adrenaline (5×10^{-6}M.) and its combinations: ADP+adrenaline, ADP+collagen and adrenaline+collagen. Morphological itravascular of activity of thrombocytes (IAT) was defined [10]. The statistical processing of the received results is carried out with usage of Students' criteria.

Results of research

The calves with dyspepsia the increase a POL of plasma were marked. So, the concentration of TBA-active products in plasma has made 5,10±0,02 mcmole/l., in the control - 3,92±0,06 mcmole/l. The level MD in thrombocytes also has appeared is raised ($1,54\pm0,004$ nmole/10^9 thr.) and in the control ($0,89\pm0,02$ nmole/10^9 thr.), which testify to activation in its of free - radical oxidation (FRO) in connection with easing intrathrombocyte of antioxidizing activity. The contents AGP in plasma of the sick calves was 3,50±0,01 D_{233} /1 ml. (the control 1,92±0,02 D_{233} /1 ml. Into thrombocytes of the sick calves AGP ($3,49\pm0,01$ $Д_{233}$ /10^9 thr.) also essentially exceeded control parameters ($2,87\pm0,04$ D_{233} /10^9 thr.).

The activation thrombocytes POL in the sick calves became possible as a result of essential slackening antioxidizing enzymes of platelets - SOD - $1250,0\pm4,36$ IU/10^9 thr. (the healthy calves $1780,0\pm2,06$ IU/10^9thr.) and catalase - $5690,0\pm21,0$ IU/10^9thr. (in group of comparison $10500,0\pm 11,05$ IU/10^9thr.). The level average molecules in plasma at 280 nm. made 0,49±0,01u.e., at 254 nm. - 0,32±0,02u.e., against the control 0,32 ±0,002u.e. and 0,24±0,03u.e., accordingly. Into thrombocytes of calves with dyspepsia average molecules have made at 280nm. - $0,061\pm0,02$ u.e./10^9 thr., at 254nm. - $0,069\pm0,03$u.e./10^9 thr. (in the control

$0,050\pm0,04$u.e./10^9 thr. and $0,055\pm0,0403$ u.e./10^9 thr., accordingly).

The research of lipide composition of membranes thrombocytes at the sick calves has revealed decrease of the contents in its phospholipids up to $0,38\pm0,001$ mcmole/10^9 thr., and increase of a level cholesterin up to $0,82\pm0,001$ mcmole/10^9 thr. In the control the similar parameters have made $0,49\pm0,002$ mcmole/10^9 thr. and $0,73\pm0,001$mcmole/10^9 thr., accordingly. For the sick animals the intensifying thromboplastinoformation was marked. The time of formation active thromboplastin made $2,95\pm0,01$mines., activity - $9,6\pm0,02$ sec. In group of the control thromboplastin was formed for $2,40\pm0,01$mines., and the activity made $14,0\pm0,05$ sec.

All complex of biochemical changes in thrombocytes characterized hypermetabolism of arachidonic acid in its and increase thromboxanoformation. In simple sample of carrying the level thromboksan in platelets the calves is indirectly appreciated - $74,3\pm0,03$ % (in the control - $39,2\pm0,02$%). These parameters speak about activation cyclooxygenase, revealed on restoration AT in collagen - aspirinum sample - $96,8\pm0,05$ % and thromboksansynthetase, detected on restoration AT in collagen - imidazole sample - $54,6\pm0,02$ %, for healthy animals – $78,4\pm0,19$ and $30,3\pm0,01$ %, accordingly.

The quantity thrombocytes in blood of the patients was within the limits of norm. The acceleration AT was marked, especially under influence collagen - $25,3\pm0,20$ sec. (control - $30,0\pm0,12$sec.). A little bit more slowly AT developed at calves under influence ADP ($33,0\pm0,12$ sec.) and ristomycinum ($26,2\pm0,13$ sec.), in the control - $39,0\pm0,28$ sec. and $41,0\pm0,26$ sec., accordingly. Thrombinum and adrenalinum AT developed faster, than the control and were equal $42,4\pm0,11$ sec. and $75,6\pm0,16$ sec., accordingly ($P < 0,01$). The time of development AT under influence combined of application inductors also was accelerated. ADP+adrenaline адреналин - $20,0\pm0,12$ sec., ADP+collagen - $18,0\pm0,09$ sec., adrenaline+collagen - $20,3\pm0,07$ sec.

Intravascular thrombocytes activity of the patients was characterized by its increase. Diskocytes in blood of the sick calves have made $62,0\pm0,20$ % (in the control - $82,0\pm0,16$ %). The quantity disko-echinocytes was increased ($18,0\pm0,40$ %). The contents spherocytes, spheroehinocytes and bipolar forms thrombocytes also considerably exceeded control parameters: $12,0\pm0,03$ %, $6,0\pm0,02$ % and $2,0\pm0,01$ % accordingly The sum of the active forms thrombocytes of the patients was equal $38,0\pm0,30$ %, the control - $18,0\pm0,20$ %, small and large aggregates contained $15,2\pm0,06$ and $4,7\pm0,03$, in the control - $3,6\pm0,04$ and $0,12\pm0,01$, accordingly, at the same time the quantity thrombocytes in aggregates at the sick animals reached $14,6\pm0,02$ %, against $5,0\pm0,20$ % in the control.

Discussion

The current dyspepsia the calves carries complex character and is accompanied by development thrombocytopathy and activation of process of coagulation blood. Pathogeny of dyspepsia causes shifts in the ratio cholesterin/phospholipids into thrombocytes membranes, that in aggregate with infringements of digestion and adsorption the POL promotes to increase in current of blood, and then and in thrombocytes of the contents average molecules, causing easing antioxidantic of protection blood platelets and increase of concentration in them of primary and secondary products. In these conditions at calves there is an activation thrombocytes and thromboplastinoformation. The increase of thrombogenic potential of blood plasma for dyspepsia is connected first of all to activation platelet functions, instead of with increase of levels of the various factors of curtailing, including fibrinogenum. The activation fibrinoformation, undoubtedly having a place at dyspepsia, occurs first of all on a surface activated thrombocytes and carries always secondary character in relation to them adhesion and aggregation intensifying.

Set of metabolic infringements, change of structure of thrombocytes membranes, increase of the contents in them average molecules and intensifying intrathrombocyte the POL results in increase LAT, increasing the contents of the active forms of blood platelets in current of blood. High LAT causes aggregative activity of thrombocytes under influence various inductors intensifying. As possible mechanisms of this intensifying it is possible to consider activization of an exchange arachidonic acid with increase thromboxanoformation, registered in tests of carry and increase of concentration participating in process aggregation of Willebrand factor,

indirectly appreciated on acceleration AT with ristomycinum.

The research сочетанного of influence inductors on process AT at the sick calves has shown them interpotentiation action. The registration AT under influence of a combination two индукторов allows to come nearer to understanding of real conditions current of blood the animal with dyspepsia and testifies to expediency of purpose of the appropriate therapy capable to normalize hemorheology.

The revealed infringements thrombocyte hemostasis at calves with dyspepsia require adequate correction directed on break of „vicious circles", developing at dyspepsia.

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The summary

At newborn calves with dyspepsia the increase aggregative function of thrombocytes in vitro and in vivo is revealed. In a basis of these infringements the deep shifts of lipide structure of membranes thrombocytes, increase of the contents in plasma and in blood platelets of level average molecules, activation of peroxide oxidation of plasma lipids, intensifying of synthesis in a wall of vessels of Willebrand factor and intensification thromboxanoformation in blood platelets lay. The activation thromboplastinoformation is the conducting reason of increase of curtailing of blood at newborn calves with dyspepsia. The correction of infringements thrombocyte of a link hemostasis should include pathogeneticly the caused complex capable to reduce a level of average molecules in organism and to treat dyspepsia.

SMOOTH MYOCYTES IN THE AORTIC VALVE

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Condition of the problem.

The passive functioning, limiting of the retrograd blood flow and movements of the valves of heart by the gradient of blood pressure are accepted as correct. But the last years investigations call the rigidity of the same affirmations into question. Thus T.H. Williams & J.Y. Jew [3] have found the cardiomyocytes, smoth myocytes and interstitial cells and also nervous fibers in mitral valves of the rat's hearts. M. Cimini et al. [1] have described the smooth myocytes in semilunar valves of hearts of human

and pig. A. Deb eat al [2] affirm that fibroblasts, originated from bony marrow locate in the cardiac valves of adult man.

Take into consideration an important role of aortic valve in the blood flow organization, the work with the aim to study the structural bases of its semilunar cuspsmovements was fulfiled.

Matherial and methods.

The investigation was carried out on 20 adult human cadavers and 30 both sexes white rats of 5-12 monts old. Semilunar cusps of a valve were choosed from the aortic wall, serial longitudinal (from base to tip) and transverse (in plane of the stretched cusp) histological sections (5-10 mkm in thickness) were made. Sections were stained by picrofuxine by VanGieson and Verhoef methods. The electron microscopic investigation of the rat's aortic valve was also carried out, at that its the nearest to free border thin area was collected.

Results.

Smooth myocytes were determined in the aortic valve fom the base up to free border of cusp. In the much more great human valve the quantity and sizes of smooth myocytes larger than in rat.

Smooth myocytes irregular distribute in thickness of rte aortic valve and by its length. They have primary transverse and oblique transverse orientation. Muscular bundles are arcuated as a parabola in the base of valve. Their branches pass through lateral segments of each semilunar cusp to its free border. Large myocytes form the multylayer stratum in the base of valve – valvar roller. In direction to free border of the semicircular cusp, the quantity of muscular layers and also theis thickness and compactness decrease. Thinning, dispersion and straightening of muscular bundels becoming parallely to free border take place. In contrast to thick valvar roll, the thinning cusp contains the gradually loosening network with different orientated myocytes. Longitudinal and oblique-longotudunal bundles are better appeared in the axial (inner) sector of valve (Figure 1). But even the continous muscular layer appears near the free border of valve (Figure 2).   Smooth myocytes are surrounded by their's own basal membrane and bundles of connective tissue fibers, the connective tissual cell can divide them from endothelium (Figure 3).

Conclusion.

The results of the realized investigation evidens that aortic vcalve contains the great number of smooth myocytes, but their distribution in thickness and length of semilunar cusp is irregular such as a whole valve constuctionis unequal. The fixed parietal part of valve (roll) counteracts to blood flow by its strustures thickening, compacting and interlacing. The free luminar part of valve (cusp) is movable and is able to react on the blood pressure by displacing and contortioning. Dispersioning and decreasing of muscular structures in the direction from base to free border of the cusp are possible to be explained by the functional load decreasing. Concentration and enlargening of the smooth myocytes near the free border of cusp may be determined by the local increasing of load on it in situation of locked valve: the retrograde blood flow contains to act on the thightly locked (fixed) free borders of semilunar cusps. Longotudinal blows of direct blood flow stimulate the development of musculo-elastic complex and longitudinal structures in the axial sector of cusp.

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Signatures to figures of the paper of V.M. Petrenko "Smooth myocytes in the aortic valve":
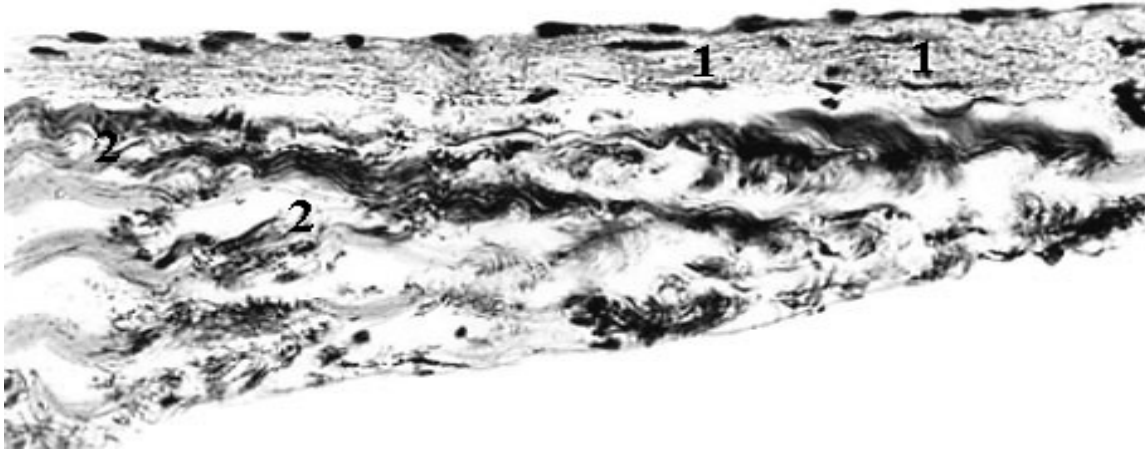
Figure 1. Aortic valve of man, longitudinal section:
1 – longitudinal myocytes in axial sector; 2 – myocytes between fold-liked bundles of collagen fibers of the parietal sector. Picrofuxine. x 200.
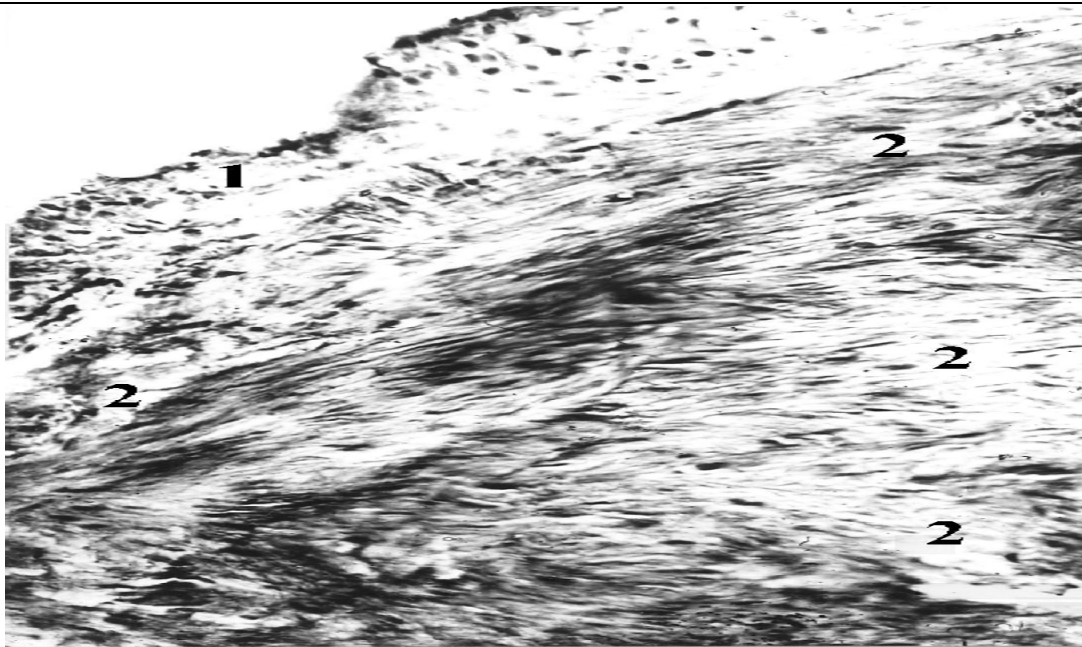
Figure 2. Aortic valve of rat, section in the plane of cusp:
1 – endothelium of the free border; 2 – intimating bundles of myocytes. Picrofuxine. x 400.
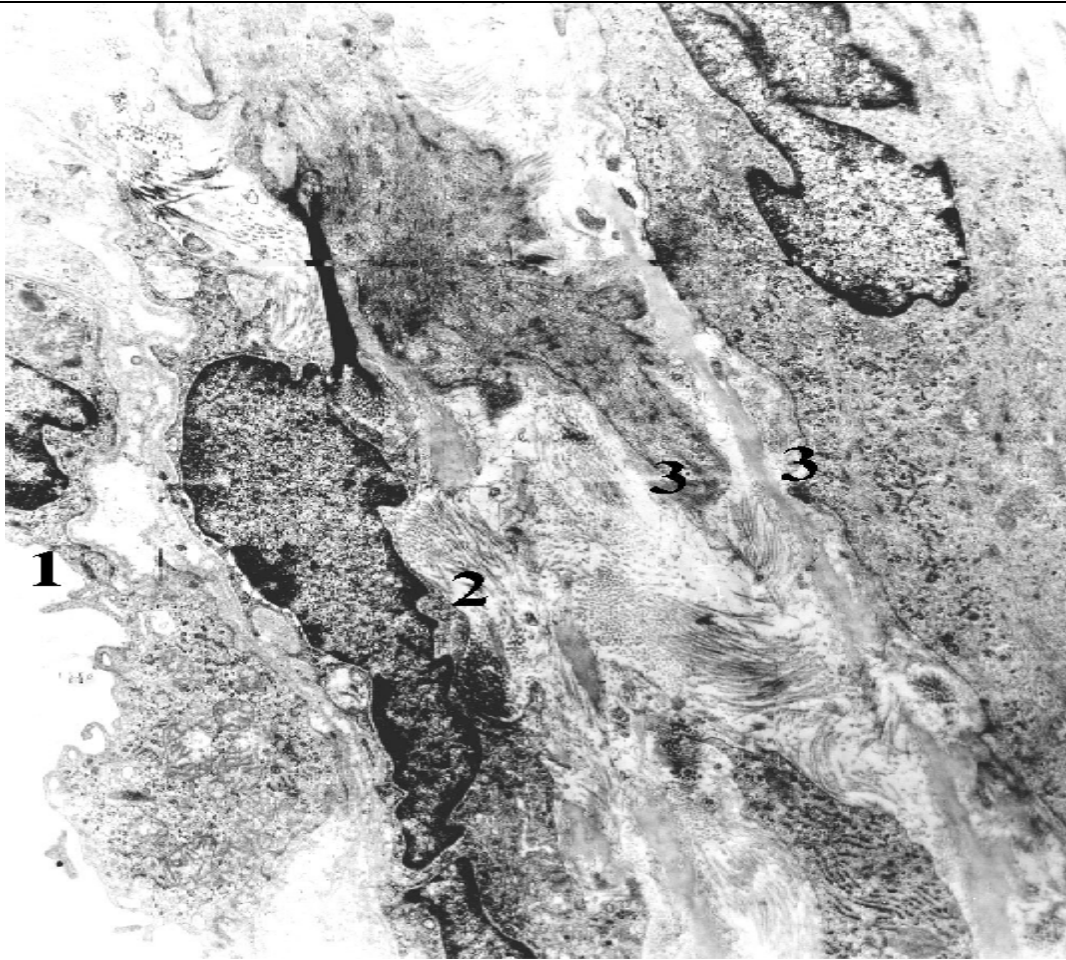
Figure 3. Aortic valve of rat, electron microscopic picture: 1 – endotheliocyte; 2 – connective tissual cell; 3 – smooth myocytes. x 10000.

Materials of the Conferences

ABOUT THE THEOREM OF SOKHOTSKY-WEIERSTRASS TYPE FOR TRIANALYTIC FUNCTIONS

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The classification of isolated singular points [5-7] of poly-analytic functions [3-5, 10], appearing due to the theorem of Sokhotsky-Weierstrass type [1, 2-5, 10], does not exclude the possibility of its being worked out in detail for some

$$F(z) = f_0(z) + f_1(z)\bar{z} + f_2(z)\bar{z}^2, \qquad (1)$$

prescribed in some deleted neighborhood of this point, consists of a point (finite or infinite), or a line of the plane $\overline{\mathbf{C}}$, or grouping of two lines, or a half-line, or a parabola of the second order, or a circle, or a Pascal snail of any of the four kinds with the isolated point elimination, or finally, is total, i.e. coincides with the whole plane $\overline{\mathbf{C}}$; here and further the lines, half-lines and parabolas of the plane $\overline{\mathbf{C}}$ being considered as completed with ∞ point.

Vice versa, for a point $a \in \overline{\mathbf{C}}$ and a set $\Phi \subset \overline{\mathbf{C}}$, which is a line or a grouping of two arbitrary lines (parallel or concurrent), or a half-line, or a parabola of the second order, or a circle, or a Pascal snail of any of the four kinds with the isolated point elimination, or finally, for $\Phi = \{c\}$ with *c* as an arbitrary point of the plane $\overline{\mathbf{C}}$, a tri-analytic function $F(z)$ with analytical components – rational functions from the field $\mathbf{C}(z)$, for which $C(F(z), a) = \Phi$, exists.

Deduction

If the point $a \in \overline{\mathbf{C}}$ is an essentially singularity for at least one analytic function $f_k(z)$ $(k = 0,1,2)$, it is the only case when $C(F(z), a)$ is total, i.e. coincides with $\overline{\mathbf{C}}$ [3-4, 7].

Now let the point $a \in \overline{\mathbf{C}}$ be not an essential singularity for none of the analytic

particular kinds of these functions, for example, for those of them, the structure of limit sets in l-points and o-points of which can be specified. In particular, such a specification can be offered for tri-analytic functions [8, 9], as a theorem, which is a nontrivial specifying and adding to a corresponding theorem for poly-analytic functions, is possible to be established for them.

Theorem

A limit set in an arbitrary point $a \in \overline{\mathbf{C}}$ of any tri-analytic function

components $f_k(z)$ $(k = 0,1,2)$ of the tri-analytic function $F(z)$, but then a representation (3) of [10] takes place, if $a = \infty$, or an analog representation for the function $F(z) = F(z + a)$ in some deleted neighborhood of the null point. Now the structure of the limit set $C(F(z), a)$ will be fully defined by the corresponding functions $F_\infty(z)$ и $F_w(z)$ [5, 10] (the function $F_0(z)$ can be ignored, as $C(F_0(z), a) = \{0\}$).

If $F_\infty(z) \equiv 0$, and $F_w(z) \equiv c \in \mathbf{C}$, then $C(F(z), a) = \{c\}$; and if $F_\infty(z) \equiv 0$ and $F_w(z)$ is not identical to the constant, then $C(F(z), a) = P(w)$ where $w = \{z : |z| = 1\}$ is a unit circle and $P(z) = a_{(-2,2)}z^2 + a_{(-1,1)}z + a_{(0,0)}$ is a first or second degree polynomial [5, 9, 10] from the ring $\mathbf{C}[z]$. In the first case $P(w)$ is, obviously, a circle; and in the second one – a Pascal snail of any of the four kinds [11] or again a circle.

The given conclusion for the second case results from an easily fixed auxiliary fact.

Lemma

The image of the circle $w = \{z : |z| = 1\}$ with mapping given by a second degree

polynomial $P(z) = Az^2 + Bz + C$ will be:

with $B = 0$ - a circle of radius $|A|$ and centre O;

with $B \neq 0$ - a Pascal snail (with its isolated point elimination), the snail having a juncture if $|B| < 2|A|$; the snail being a cardioid with a cuspidal point if $|B| = 2|A|$; the snail having the only point in which right and left tangents coincide (and the snail will have two flex points) if если $2|A| < |B| < 4|A|$; the snail having the only one tangent in its every point, but not having a cuspidal point if $|B| \geq 4|A|$.

Deduction

Taking $A \neq 0$ and $B \neq 0$, let us assume the polynomial $P(z) = Az^2 + Bz + C$, $A \neq 0$ as follows

$$P(z) = A\left(z + \frac{B}{2A}\right)^2 + C - \frac{B^2}{4A}.$$

Now let us write a nonvanishing number $\frac{B}{2A}$ in an exponential form $\frac{B}{2A} = re^{ij}$ with $r = \left|\frac{B}{2A}\right| > 0$, $0 \leq j < 2p$, and finally, reduce the polynomial to the form

$P(z) = Ae^{2ij}(ze^{-ij} + r)^2 + C - Ar^2 e^{2ij}$ .Now, obviously, it is enough to clear up what is the image of the unit circle $w = \{z : |z| = 1\}$ with mapping given by the following auxiliary polynomial: $\tilde{p}(z) = (z + r)^2$, with $r > 0$; but if $z = e^{it}$ with $0 \leq t < 2p$, then

$\tilde{p}(z) = (e^{it} + r)^2 = (\cos t + i\sin t + r)^2 =$

$= 2\cos^2 t + 2r\cos t + r^2 - 1 + 2i(r + \cos t)\sin t$,

that means [11]: $\tilde{p}(w)$ is a Pascal snail (with the isolated point elimination) with the parameters $a = 2$ and $l = 2r$, which is biased to the vector $(r^2 - 1; 0)$. The lemma is proved.

Now let the function $F_\infty(z)$ be not identical to the constant. Then $C(F(z), a) = \{\infty\}$ or $C(F(z), a)$ is a join of a finite number of nontrivial polynomial lines augmented with ∞ point. The last situation for tri-analytic functions needs to be specified (1). To do it we have to change the function $F_w(z)$ with the corresponding constant [5, p. 58], then apply the described in [5] (theorem 3.1) poly-analytic property deflation mode of the function $F_\infty(z)$. The made transformations allow to make sure that the above join can be a line, or a grouping of two lines, or a half-line, or a parabola of the second order (with adding to every of these sets ∞ point).

As a supplement to the deduction of the first part of the theorem it is worth taking into account the first part of the theorem 3.2 from [5], and also the possibility to transform the case $a = 0$ to the case $a = \infty$ (and vice versa) by means of a simple change of the variables – changing symbol z into the expression $\frac{1}{z}$ and multiplying the given function by the fraction $\left(\frac{\bar{z}}{z}\right)^2$ with the further considering of this factor's possibility to converge to one of not more than two complex numbers ([5], p. 57).

The deduction of the second part of the theorem becomes easy when denoting concrete samples of realization of all the numerated in the theorem cases, the structuring of the corresponding samples being obvious or being contained in [5,6].

Note

It is obvious that the given theorem allows to offer a more delicate classification of isolated singularities of tri-analytic functions compared to the classification of these points for poly-analytic general functions, and namely, to excel, alongside with the essential singularity, removable (on continuity) singularity and a pole, four kinds of l- and o-points more.

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ABOUT SOME METHODS OF CONSTRUCTION POLYANALYTIC FUNCTIONS WITH A PREDETERMINED LIMIT SET IN THEIR ISOLATED SINGULAR L-POINT

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In this paper we consider a new method of quick construction of polyanalytic functions with a predetermined cluster set in isolated singular B-points (radiant points) of these functions.

It is known [1–5, 7] that if a set $M \subset \overline{\mathbf{C}}$ of any of the four types is given: an extended complex plane $\overline{\mathbf{C}}$, a polynomial image $P(w)$ of a unit circle $w = \{z \in \mathbf{C} : |z| = 1\}$ ($P(z) \in \mathbf{C}[z] \setminus \mathbf{C}$), an arbitrary unit subset of the set $\overline{\mathbf{C}}$, and finally, a union of finite number of nondegenerate polynomial lines $\bigcup\limits_{j=1}^{m} L_j$ augmented with ∞ point, then for any point $a \in \overline{\mathbf{C}}$ there is such a deleted neighborhood $\overset{\mathbf{o}}{O}(a)$ of its and a defined in it poly-analytic (p.a.) function $F(z)$, i.e. the function of the kind

$$F(z) = \sum_{k=0}^{n-1} f_k(z)\overline{z}^k , \qquad (1)$$

where $n \in N$, $f_k(z)$ ($k = 0,..., n-1$) – are analytic in $\overset{\mathbf{o}}{O}(a)$ functions, that $C(F(z), a) = M$. Let us remind that the number $n \in N$ is called [1] the order of poly-analytic property of the function $F(z)$, and if

$f_{n-1} \not\equiv 0$, then it is called the proximate order of its poly-analyticity; the functions $f_k(z)$ ($k = 0,..., n-1$) are called the analytic components of the poly-analytic (or as it is spoken about, n - analytic) function $F(z)$.

However, the earlier offered in [2,3] method of finding the corresponding p.a. function for the last, the fourth, case, when the point a is called [2, 3] the isolated singular 1-point of the function $F(z)$, and the predetermined set $M \subset \overline{\mathbf{C}}$ is sure to have the form

$$M = \bigcup_{j=1}^{m} L_j = \bigcup_{j=1}^{m} P_j(\overline{R}), \qquad (2)$$

where $L_j = P_j(\overline{R})$, $P_j(z) \in \mathbf{C}[z] \setminus \mathbf{C}$, $P_j(\infty) = \infty$; $j = 1,...,m$, unlike the rest of the cases, was very complicated and tedious.

In this article essentially more simple modes of construction of a p.a. function possessing a limit set of the kind (2) in its isolated 1-point are offered, $P_j(z) \in \mathbf{C}[z] \setminus \mathbf{C}$ ($j = 1,...,m$) being arbitrary predetermined polynomials different from those identical to the constants.

As compelling for any $a \in \mathbf{C}$ congruence $C(F(z), a) = C(F(z + a), 0)$ allows considering that $a = 0$ or $a = \infty$, and vice versa, then, for the sake of simplicity, some results further will be formulated namely for $a = \infty$.

Theorem 1

Let $L = \bigcup_{j=1}^{n} P_j(\overline{R})$, where $n \in N$,

$P_j(z) = c_m^{(j)} z^m + c_{m-1}^{(j)} z^{m-1} + ... + c_0^{(j)}$,

$m \in N$, $c_m^{(j)} \neq 0$, $j = 1,2,...,n$ and let $c_k^{(j)} = p_k(e_j)$, where the polynomials $p_k(z) \in \mathbf{C}[z] \setminus \mathbf{C}$, $k = 0,1,...,m$, and the numbers $e_1, e_2,..., e_n$ are all complex n-th roots of 1 (unity), the polynomial $p_m(z)$ has no complex unit module roots, then for the function

$$F(z) = p_m\left(\frac{\overline{z}}{z}\right)\left(i\overline{z}^n - iz^n\right)^m + p_{m-1}\left(\frac{\overline{z}}{z}\right)\left(i\overline{z}^n - iz^n\right)^{m-1} + ... + p_0\left(\frac{\overline{z}}{z}\right)$$

the congruence $C(F(z),\infty) = L$ is correct.

The deduction of the theorem 1 is in [6].

Samples

1. As $C(\overline{z} - z, \infty) = i\overline{R}$, then

$C\left(\overline{z}^2 - z^2 + \frac{\overline{z}}{z}, \infty\right) =$

$= (i\overline{R} + 1) \mathbf{U} (i\overline{R} - 1)$ is a union of a pair of parallels;

$C\left(i\overline{z}^3 - iz^3 + \frac{\overline{z}}{z}, \infty\right) = \overline{R} \mathbf{U}(e_1 + \overline{R}) \mathbf{U}(e_2 + \overline{R})$ is a union of three parallels

$\left(e_1 = e^{i\frac{2p}{3}}, \ e_2 = e^{i\frac{4p}{3}}\right)$;

$C\left(i\frac{\overline{z}}{z}\left(\overline{z}^3 - z^3\right), \infty\right) = \overline{R} \mathbf{U} e_1\overline{R} \mathbf{U} e_2\overline{R}$ is a union of tree concurrent in the 0 point lines.

2. As $C\left(-(\overline{z} - z)^2, \infty\right) = \overline{R}_+$, то

$C\left(\left(-(\overline{z}^2 - z^2)^2 + 1\right)\frac{\overline{z}}{z}, \infty\right) =$

$(-\infty, -1] \mathbf{U} [1; +\infty)$;

$C\left(-\frac{\overline{z}}{z}\left(\overline{z}^3 - z^3\right)^2, \infty\right) = \overline{R}_+ \mathbf{U} e_1\overline{R}_+ \mathbf{U} e_2\overline{R}_+$ is

a union of three half-lines, all of them centering in 0 point and making angles of 120^0.

3. As $C\left((\bar{z}+z+i)^2+1,\infty\right)=\left\{t^2+2ti\,|\,t\in\bar{R}\right\}$ is a parabola of the second order, then every of the sets, $C\left(\dfrac{\bar{z}}{z}\left((\bar{z}^2+z^2+i)^2+1\right),\infty\right)$ and

$C\left((\bar{z}^2+z^2+i)^2+1+\dfrac{\bar{z}}{z},\infty\right)$, is a union of two parabolas.

In the conclusion of the article let us show some simple upper estimate of the number of polynomial lines, making up $C(F(z),a)$, where $a\in\overline{\mathbf{C}}$ is isolated singular l-point of the p.a. function $F(z)$.

Theorem 2

For any p.a. function $F(z)$ of the proximate poly-analyticity order $n\in N,\ n\ge 2$, and for its every isolated singular l-point $a\in\overline{\mathbf{C}}$ the set of all the elements from $C(F(z),a)\,\mathbf{I}\,\mathbf{C}$ can be represented in the form of a union of finite number of nontrivial polynomial lines, the quantity of which $l\in N$ satisfies the following conditions:

а). $l\le 4(n-1)$;

б). $l\le (n-1)!$ (with $n=2$ and with $n=3$ this estimate is exact).

The deduction of the theorem 2 is in [6].

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CHRACTERISTIC PROPERTIES OF SEQUENCES GENERATING FINITE ELEMENTS OF POLYANALYTIC FUNCTIONS' CLUSTER SETS IN THEIR ISOLATED SINGULAR L-POINTS

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1. For every poly-analytic function (p.a. function) [1-4]

$$F(z) = \sum_{k=0}^{n-1} f_k(z)\bar{z}^k, \ n \in N, \quad (1)$$

set in a deleted neighborhood $\overset{0}{O}(a)$ of its isolated nonessential singularity $a \in \overline{\mathbf{C}}$, the

representation $F(z)$ in $\overset{0}{O}(a)$ is possible in the following form [4, 6]:

$$F(z) = F_\infty(z) + F_w(z) + F_0(z), \quad (2)$$

where p.a. functions $F_\infty(z)$, $F_w(z)$ and $F_0(z)$ are identically determined [4, 6] by expansion coefficient of analytic in $\overset{0}{O}(a)$ functions $f_k(z)$ $(k = 0,...,n-1)$ in a Laurent series. Functions $F_\infty(z)$, $F_w(z)$ and $F_0(z)$ allow to describe identically a cluster set [1, 2, 4, 6] $C(F(z),a)$ of a poly-analytic function $F(z)$ in a point $a \in \overline{\mathbf{C}}$, in particular, to

establish if the a point is an isolated l-point for $F(z)$; [4, 6], without loss of reasoning generality, being always possible to pass on from studying the behaviour of an arbitrary p.a. function $F(z)$ in a deleted neighborhood $\overset{0}{O}(a)$ of its isolated singular l-point $a \in \overline{\mathbf{C}}$ to studying of the behaviour of a poly-analytic polynomial $P(z,\bar{z}) \in \mathbf{C}[z,\bar{z}] \setminus \mathbf{C}$, i.e.

$$P(z,\bar{z}) = p_0(z) + p_1(z)\bar{z} + ... + p_{m-1}(z)\bar{z}^{m-1}, \quad (2)$$

$(p_j(z) \in \mathbf{C}[z]; \ j = 0,...,m-1)$, in the neighbourhood of ∞ point; besides

$$C(F(z),a) = \bigcup_{j=1}^{m-1} (C(P(z,\bar{z}),\infty) + c_j),$$

where $c_j \in \mathbf{C}$ $(j = 1,..., m-1)$, $0 < m < n$, $m \in N$.

In the clauses [3, 4] it was got the criterion of availability of the not identical to the constant p.a. polynomial (2) of finite limited values in ∞ point; the speciality of getting this criterion being that, that allows describing all the sequences generating all finite limited values in ∞ point of the p.a. polynomial;

and it means it allows describing all the sequences generating all the finite limited values of an arbitrary p.a. function in its any isolated singular l-point.

2. To formulate the corresponding results, let us enter some auxiliary notions; besides let us suppose further that for any element $l \in \overline{\mathbf{C}}$ any sequence of complex numbers convergent to l is considered to be known.

Definition 1

About the sequence of complex numbers (z_n) we shall speak that it is made up of the sequences

$$(z_n^{(1)}), (z_n^{(2)}),...,(z_n^{(s)}), \quad (3)$$

if every component of any of the sequences of the set (3) is the component (and the only one component) of the sequence (z_n), and there are no other components in this sequence.

Thus, either any two components of different sequences from (3) or two any components of different numbers of the same sequence from (3)will turn out to be different components of the

sequence (z_n); the values of the components of these sequences being not considered.

Now, taking into account that any sequence of complex numbers has a convergent subsequence (to the finite element from $\overline{\mathbf{C}}$ or to ∞) and that any sequence (z_n) possessing the property $p(z_n) \to 0$ where $p(z)$ is some not identical to the constant analytic polynomial from z, is limited, and also that this polynomial $p(z)$ has a nonempty finite collection of roots in $\overline{\mathbf{C}}$, it is possible to formulate the following lemma.

Lemma 1

For any not identical to the constant analytical polynomial $p(z)$ the sequence of complex numbers (z_n) possesses the property $p(z_n) \to 0$ when and only when it is made up of an arbitrary part of the finite set of any sequences, every one of which converges to one of the roots of the polynomial $p(z)$.

It is relevant, in addition to the notion of the composed sequence (or even just as another way to describe resembling situations), to formulate the notion of the sequence convergent to a finite set and the corresponding property (lemma 2).

Definition 2

About the sequence of complex numbers (z_n) we shall speak that it converges to a nonempty infinite set $M = \{m_1, m_2, ..., m_k\} \subset \mathbf{C}$, if for any set

$$O_e(M) = \bigcup_{s=1}^{k} O_e(m_s) \quad \text{where} \quad O_e(m_s) \quad \text{is}$$

any e-neighbourhood of the point m_s $(s = 1, ..., k)$, there is such a number $n_0(e)$ that for any natural n, if $n > n_0(e)$, then $z_n \in O_e(M)$; if the sequence (z_n) converges to M, but doesn't converge to any of its eigenparts, then we shall speak about the sequence (z_n), that it converges to all the set M.

The following lemma 2 is evident.

Lemma 2

Any sequence of complex numbers (z_n) possesses the following property $p(z_n) \to 0$, where $p(z)$ is some not identical to the constant analytical polynomial, when and only when it converges to the set (not obligatory to the whole one) of all complex roots of the polynomial $p(z)$.

The fact, that the notions of the composed sequence and the sequence convergent to a set, is directly relevant to establishing the characteristic property of sequences generating finite limited values of p.a. polynomials in ∞ point, will be evident after establishing the following fact (theorem 1), that, however, is necessary to precede with some agreements about the nomenclature.

3. Let $P(z, \overline{z})$ be an arbitrary p.a. polynomial of the form (2) and not identical to the constant, and let

$$p_j(z) = c_0^{(j)} + c_1^{(j)} z + ... + c_{k_j}^{(j)} z^{k_j}, \quad (j = 0, ..., m-1)$$

In addition to it let us consider that $P(z, \overline{z})$ informally depends both on z and on $\overline{z}$, i.e. $P(z, \overline{z}) \in \mathbf{C}[z, \overline{z}]$, but $P(z, \overline{z}) \notin \mathbf{C}[z]$ and $P(z, \overline{z}) \notin \mathbf{C}[\overline{z}]$.

Let us mention that it won't violate the reasoning generality, as for any not identical to the constant polynomial from the ring $\mathbf{C}[z]$ or from the ring $\mathbf{C}[\overline{z}]$, its cluster set in ∞ point is settled with one ∞ element.

Let it further be that $s = \deg_{z, \overline{z}} P(z, \overline{z}) \in N$.

Besides (for the nomenclature brevity sake) let us agree to add formal summands with trivial coefficients to any from the polynomials $p_j(z)$ as far as possible, and let us consider from now that $k_j + j = s$ $(j = 0, ..., m-1)$, but at least one of the coefficients $c_{k_j}^{(j)}$ is nonzero.

Let us denote now a p.a. polynomial composed of all monomials of the p.a. polynomial (2) $P(z,\overline{z})$ of the form $c_{k_j}^{(j)} z^{k_j} \overline{z}^{s-k_j}$, $(j=0,...,m-1)$ by the symbol $\widetilde{P}(z,\overline{z})$, i.e.

$$\widetilde{P}(z,\overline{z}) = \sum_{j=0}^{m-1} c_{k_j}^{(j)} z^{k_j} z^{s-k_j}.$$

It is evident that

$$\widetilde{P}(z,\overline{z}) = z^s \cdot \sum_{j=0}^{m-1} c_{k_j}^{(j)} \left(\frac{\overline{z}}{z}\right)^{s-k_j} = z^s \cdot P\left(\frac{\overline{z}}{z}\right),$$

where $P(w)$ is a not identical to the constant analytical polynomial from w, then the following statement makes sense.

Theorem 1

Every sequence of complex numbers (z_n) generating a finite point of a cluster set in ∞ point of the not identical to the constant p.a. polynomial $P(z,\overline{z})$ possesses the following property: the sequence $\left(\dfrac{\overline{z}_n}{z_n}\right)$ converges to the set of all roots of a unit module of the analytic polynomial $P(w) \in \mathbf{C}[w] \setminus \mathbf{C}$.

Deduction

Let $P(z,\overline{z})$ be a p.a. polynomial differing the not identical to the constant one, and let a sequence of complex numbers (z_n) possesses properties: $z_n \to \infty$, and $(P(z_n,\overline{z}_n))$ converges to

the finite limit, but then $\dfrac{P(z_n,\overline{z}_n)}{z_n^s} \to 0$, but $\left|\dfrac{\overline{z}_n}{z_n}\right| \equiv 1$, that proves the theorem.

Complementation

If a polynomial $P(w)$ constructed not for the identical to the constant p.a. polynomial $P(z,\overline{z})$ has no roots of a unit module, then $C(P(z,\overline{z}),\infty) = \{\infty\}$.

Theorem 1 allows concluding that every sequence of complex numbers (z_n) generating a finite limited value of the not identical to the constant p.a. polynomial in ∞ point is made up of a part of a finite set of sequences (their own for every (z_n)) $\left(z_n^{(j)}\right)$ of which every one converges to ∞, simultaneously "ranging" in the direction set by a straight line from the finite collection (for every $\left(z_n^{(j)}\right)$ a straight line from this collection is its own and it is possible to consider that it passes through the point $z=0$). The "structure" of every of the sequences $\left(z_n^{(j)}\right)$ was studied in [3] and [4], that allows formulating the following theorem; the situation for b.a. functions is fully considered in [3, 7].

Theorem 2

For any p.a. function $F(z)$ of poly-analyticity order $n \geq 2$ and its any isolated singular l-point $a \in \overline{\mathbf{C}}$ there is a finite collection of expressions of the following form:

$$z^{(j)}(x,t) = d_j + c_j\left(b_j + a_j\left(x + i \cdot \frac{t - P_j(x)}{x^{d_j}}\right)^{l_j}\right) \quad (j=1,...,s; \ s \leq n-1), \quad (4)$$

where complex numbers d_j, c_j, b_j, a_j $(c_j, a_j \neq 0)$ as well as the coefficients of the polynomials $P_j(x)$ from the ring $R[x]$, are fully determined by the coefficients of analytic components of the p.a.

function $F_\infty(z)$ corresponding to the p.a. function $F(z)$ and the point $a \in \overline{\mathbf{C}}$, besides $l_j, d_j \in N$, $\deg P_j(x) < d_j$ $(j=1,...,s; \ s \leq n-1)$; this collection of expressions (4) possessing the following properties:

1) For any finite limited value l in the point a of this p.a. function $F(z)$ any generating

being obtained by substitution into the expressions (4) of some convergent real sequences $\left(x_n^{(j)}\right)$ and $\left(t_n^{(j)}\right)$; $\left(t_n^{(j)}\right)$ converging to some finite , and $\left(x_n^{(j)}\right)$ - to infinite limits;

2) Vice versa: for any convergent real-valued sequences (x_n) and (t_n), where (t_n) converges to an arbitrary finite, and (x_n) - to infinite limits, every of the sequences (5) generates a finite limited value of the p.a. function $F(z)$ in its isolated singular 1-point $a \in \overline{\mathbf{C}}$ (with $a = \infty$ or $a \in \mathbf{C}$ accordingly).

this point sequence (z_n) is made up of a part of the collection of sequences

$$\left(z^{(j)}\left(x_n^{(j)}, t_n^{(j)}\right)\right) \quad \text{with} \quad a = \infty, \quad \text{or}$$

$$\left(\frac{1}{z^{(j)}\left(x_n^{(j)}, t_n^{(j)}\right)} + a\right) \text{ with } a \in \mathbf{C}, \qquad (5)$$

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CLUSTER SETS OF BIANALYTIC FUNCTIONS IN THEIR ISOLATED SINGULARITIES

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Brief
General methods of finding an explicit cluster set of any bi-analytic function in its arbitrary isolated singularity.

1. Let it be required to find a cluster set $C(F(z), a)$ [1-6] of an arbitrary bi-analytic function (b.a. function) [2-6]

$$F(z) = f_1(z)\overline{z} + f_2(z) \qquad (1)$$

in its isolated singular point $a \in \overline{\mathbf{C}}$, where the functions $f_1(z)$ and $f_2(z)$ are arbitrary analytic functions in a deleted neighborhood $\overset{o}{O}(a)$ of the point $a \in \overline{\mathbf{C}}$ (so called analytic components of the b.a. function $F(z)$).

The first step in finding $C(F(z), a)$ should be most reasonable to make determining the fact if the point $a \in \overline{\mathbf{C}}$ is an isolated singularity at least for one of the functions – analytic components of the function $F(z)$, as the following result [2-4] makes sense.

Lemma 1

If the point $a \in \overline{\mathbf{C}}$ is an essential isolated singularity for at least one of the functions $f_j(z)$ $(j = 1,2)$, then $C(F(z), a)$ is total (i.e. coincides with $\overline{\mathbf{C}}$, where $F(z)$ in a b.a. function (1) given in a deleted neighborhood $\overset{o}{O}(a)$ of the point a.

2. Lemma 1 allows considering only those cases, when the isolated singularity $a \in \overline{\mathbf{C}}$ of the b.a. function $F(z)$ is not an essential singularity for $f_1(z)$ and $f_2(z)$; besides, in this case we are always successful in converting finding $C(F(z), a)$ to finding a cluster set in the point ∞ of a bi-analytic first-degree polynomial (i.e. a function from the ring $\mathbf{C}[z, \overline{z}]$) relative $\overline{z}$ or a function of the form $\dfrac{\overline{z}}{z}$ [5, 6, 10]. The following rather simple properties will help such changing.

Property 1

For any function $w(z)$ given in an unlimited set $D(w) \subset \mathbf{C}$ (i.e. $\infty \in \overline{D(w)}$) and for any polynomial $p(z) \in \mathbf{C}[z] \setminus \mathbf{C}$
$$C(w(z), \infty) = C(w(p(z)), \infty),$$
in particular
$$C(w(z), \infty) = C(w(az + b), \infty),$$
where $a, b \in \mathbf{C}$ and $a \neq 0$.

Property 2

For any function $w(z)$ given in an unlimited set $D(w) \subset \mathbf{C}$ and for any polynomial
$$p(z) = a_n z^n + \ldots + a_1 z + a_0 \in \mathbf{C}[z],$$
$a_n \neq 0$, $n \in N$, the congruence is valid:
$$C(p(z) \cdot w(z), \infty) = C(a_n z^n \cdot w(z), \infty).$$

Property 3

For any defined and continuous in $\mathbf{C}$ function $w(z)$, any point $a \in \overline{\mathbf{C}}$ and any function $j(z)$ of complex variable z the congruence is valid:
$$C(w(j(z)), a) \setminus \{\infty\} = w(C(j(z), a)) \setminus \{\infty\},$$
in particular, if $w(z)$ is an arbitrary polynomial $P(z)$ from $\mathbf{C}[z] \setminus \mathbf{C}$, then
$$C(P(j(z)), a) = P(C(j(z), a)),$$
where $j(z)$ is a function defined in a deleted neighborhood $\overset{o}{O}(a)$ of the point $a \in \overline{\mathbf{C}}$ (a natural agreement that $P(\infty) = \infty$ being accepted).

Property 4

For any function $F(z)$ with $D(F) \subset \overline{\mathbf{C}}$ and any $a \in \mathbf{C}$ the congruence is valid:
$$\mathbf{C}(F(z), a) = C(F(z + a), 0).$$

Points

Property 4 evidently always allows passing on from the research of a cluster set of an arbitrary b.a. function in its arbitrary isolated singularity $a \in \overline{\mathbf{C}}$ to the research of a cluster set of a b.a. function in its isolated singularity $a = \infty$ or $a = 0$; besides, a transition to any of these two variants is always possible [10]. Let us further suppose that $a = \infty$.

Property 5

For any complex-valued functions $w_1(z)$ and $w_2(z)$ with unlimited $D(w_1) = D(w_2) \subset \mathbf{C}$, if
$$C(w_2(z), \infty) = \{a\} \quad \text{with} \quad a \in \mathbf{C}, \quad \text{then}$$
$$C(w_1(z) + w_2(z), \infty) = C(w_1(z), \infty) + a; \quad \text{if}$$
$a \neq 0$, then
$$C(w_1(z) \cdot w_2(z), \infty) = a \cdot C(w_1(z), \infty).$$

The following fact arises from Property 5 (generalizing of Property 2).

Property 6

For any complex-valued functions $w_1(z)$, $w_2(z)$ and $w_3(z)$ defined in one and the same unlimited set of the plane $\mathbf{C}$, if

$$\lim_{z\to\infty}\frac{w_1(z)}{w_2(z)}=1,$$

then $C(w_1(z)\cdot w_3(z),\infty)=C(w_2(z)\cdot w_3(z),\infty)$.

Property 7

For any complex-valued functions $w_1(z)$, $w_2(z)$ and $w_2(z)$ defined in an unlimited set of the plane $\mathbf{C}$, if

$$\lim_{z\to\infty}\frac{w_1(z)}{w_2(z)}=\infty,$$

then

$$C((w_1(z)+w_2(z))\cdot w_3(z),\infty)=C(w_1(z)\cdot w_3(z),\infty)$$

The analogous property can be formulated for complex-valued functions of two real variables as well.

Property 8

For any complex-valued functions $A(x,y)$, $B(x,y)$ and $F(x,y)$ of two real variables x and y with coinciding domains, for which the point $(a_1,a_2)\in \overline{R}^2$ is a cluster one, if

$$\lim_{x\to a_1, y\to a_2}\frac{B(x,y)}{A(x,y)}=0,$$

then

$$C((A(x,y)+B(x,y))\cdot F(x,y),(a_1,a_2))=C(A(x,y)\cdot F(x,y),(a_1,a_2))$$

3. Let $F(z)$ be a b.a. function of the form (1) given in a deleted neighborhood of the point $a=\infty$; ∞ point not being an essential singularity for analytic components of this b.a. function, then the following representation in some $\overset{o}{O}(\infty)$ is valid for it:

$$F(z)=F_\infty(z)+F_w(z)+F_0(z),\qquad(2)$$

where

$$F_\infty(z)=(a_k z^k+...+a_1 z+a_0)\overline{z}+(b_m z^m+...+b_1 z);\qquad(3)$$
$$F_w(z)=a_{-1}z^{-1}\overline{z}+b_0;$$
$$F_0(z)=(a_{-2}z^{-2}+a_{-3}z^{-3}+...)\overline{z}+(b_{-1}z^{-1}+b_{-2}z^{-2}+...),$$

where $a_k,...,a_0,a_{-1},...$ and $b_m,...,b_0,b_{-1},...$ are corresponding Laurent series expansion coefficients in the neighborhood of the point $a=\infty$ of the analytic components $f_1(z)$ and $f_2(z)$ of the b.a. function $F(z)$, i.e.

$$f_1(z)=\sum_{j=k}^{-\infty}a_j z^j,\text{ where}$$

$k\in Z,\ a_j\in\mathbf{C}(j=k,...,0,-1,...);$

$$f_2(z)=\sum_{j=m}^{-\infty}b_j z^j,\text{ where}$$

$m\in Z,\ b_j\in\mathbf{C}(j=m,...,0,-1,...).$

As it is evident that $\lim_{z\to\infty}F_0(z)=0$, then $C(F(z),\infty)=C(F_\infty(z)+F_w(z),\infty)$ and it is natural to consider two possible situations for $F_\infty(z)$:

a) $F_\infty(z) \equiv 0$ and then $C(F(z),\infty) = C(F_w(z),\infty) = a_{-1}w + b_0$, where $w = \{z \in \mathbf{C} \mid |z| = 1\}$ is a unit circle of the plane $\mathbf{C}$, $a_{-1} \neq 0$. In this case ∞ point for $F(z)$ is called an isolated singular O-point [6-8]. But if $F_\infty \equiv 0$ and, moreover, $a_{-1} = 0$, then $C(F(z),\infty) = \{b_0\}$ and ∞ point is called a removable isolated point of the function $F(z)$ [6-8].

b) $F_\infty(z) \not\equiv 0$. In this case the properties of this b.a. polynomial $F_\infty(z)$ will be determining in the structure $C(F(z),\infty)$; the influence of the function F_w on $C(F(z),\infty)$ will be equal to a parallel translation of the set $C(F_\infty(z),\infty)$ [10].

Lemma 2

Let a bi-analytic in a deleted neighborhood $\overset{o}{O}(\infty)$ function $F(z)$ be represented in this domain in the form (2) (besides for the corresponding function F_∞: $a_k \neq 0$, $k \in N_0$, then for availability of finite elements in the cluster set $C(F(z),\infty)$ it is necessary that:

1) $k + 1 = m$;

2) $|a_k| = |b_m|$;

3) but if $k \in N$, and $a_k = b_m = 1$, then $b_{m-1} \in R$.

Points

It is obvious that for any b.a. function given in some $\overset{o}{O}(\infty)$, if the corresponding to it function $F_\infty \not\equiv 0$, then $\infty \in C(F(z),\infty)$ always.

Complementation

Let for a b.a. function $F(z)$ the corresponding to it function $F_\infty(z) \not\equiv 0$ satisfies the conditions

(1)-(2) of Lemma 2, then, if $C(F(z),\infty)$ contains finite elements, then any sequence (z_n) generating any of them satisfies the following condition:

$$\lim_{n \to \infty} \frac{\overline{z}_n}{z_n} = -\frac{b_m}{a_n}.$$

Points

The facts which are analogous to Lemma2 and the complementation to it, are obviously valid for the isolated singularity $a = 0$ as well; besides it is easy to see that the substitution of $F_w(z)$ by the corresponding constant and the substitution of z in $F_\infty(z) \not\equiv 0$ by the function $\frac{1}{z}$ with multiplying function $F_\infty\left(\frac{1}{z}\right)$ by the function of the form $A\dfrac{\overline{z}}{z}$ (where $A \in \mathbf{C}$ is selected properly [10]) allows passing on from $C(F(z),a)$ to $C(\tilde{F}(z),\infty)$, where $\tilde{F}(z)$ is a b.a. function defined in a deleted neighborhood $\overset{o}{O}(\infty)$, and moreover $\tilde{F}(z)$ is a b.a. polynomial from $\mathbf{C}[z,\overline{z}]$.

4. The following two lemmas will give us an opportunity to substantiate the theorem of Sokhotsky-Weierstrass type for bi-analytic functions fully. Besides it is worth underlying that the above points allow further formulating of many facts without loss of reasoning generality only for the case of isolated singular ∞ point of b.a. polynomials.

Lemma 3

For any bi-analytic polynomial $p(z,\overline{z})$ from $\mathbf{C}[z,\overline{z}]$ there is a certain augmented with ∞ point straight line of the plane $\overline{\mathbf{C}}$, in which there are all points from $C(p(z,\overline{z}),\infty)$.

Lemma 4

Let it for a bi-analytic polynomial

$$p(z,\overline{z}) = (a_k z^k + ... + a_1 z + a_0)\overline{z} + b_m z^m + ... + b_1 z + b_0 \in \mathbf{C}[z,\overline{z}] \setminus \mathbf{C},$$

where $k, m \in N_0$, $a_k \neq 0$, be known that $l \in \mathbf{C}$ is any its limited in ∞ point value, which is generated by a sequence (z_n), then every sequence of the form

$$(\tilde{z}_n(t)) = \left(z_n + \frac{t}{z_n^k} \right), \quad t \in \mathbf{C},$$

generates a finite point

$$l + b_m \cdot \left(t - \left(-\frac{a_k}{b_m} \right)^m \cdot \bar{t} \right),$$

of the cluster set $C(p(z, \bar{z}), \infty)$.

Complementation

If $p(z, \bar{z}) \in \mathbf{C}[z, \bar{z}] \setminus \mathbf{C}$, then $C(p(z, \bar{z}), \infty)$ either a straight line (augmented by ∞ point) or a singleton $\{\infty\}$.

The following theorem of Sokhotsky-Weierstrass type was formulated in [4], but without its full substantiating [5, 6, 10].

Theorem 1

A cluster set in any point $a \in \overline{\mathbf{C}}$ of any b.a. function (1)

$F(z) = f_1(z)\bar{z} + f_2(z)$, given in a deleted neighborhood $\overset{o}{O}(a)$ of this point a either consists of one point of the plane $\overline{\mathbf{C}}$, or represents a circle of the plane $\overline{\mathbf{C}}$, or is total, i.e. coincides with $\overline{\mathbf{C}}$. Vice versa, for any point $a \in \overline{\mathbf{C}}$ and any set $\Phi \subset \overline{\mathbf{C}}$ which is either a circle, or a straight line (augmented with ∞ point), or a one-element set (i.e. $\Phi = \{c\}$ with $c \in \overline{\mathbf{C}}$), or is the whole plane $\overline{\mathbf{C}}$, there is a defined in a deleted neighborhood $\overset{o}{O}(a)$ of the point a bi-analytic function $F(z)$, for which $C(F(z), a) = \Phi$.

5. Let us obtain the criterion which allows distinguishing if the point $a \in \mathbf{C}$ is a pole for the b.a. function given in a $\overset{o}{O}(a)$ (i.e. $C(F(z), a) = \{\infty\}$ or $C(F(z), a)$ is a straight line of the plane $\overline{\mathbf{C}}$.

To do it let us pass on to the search of a cluster set in ∞ point corresponding to the function $F(z)$ and, in general terms, an arbitrary bi-analytic polynomial $p(z, \bar{z}) \in \mathbf{C}[z, \bar{z}] \setminus \mathbf{C}$ of the form (3), as it is precisely this situation which a general case with $F_\infty(z) \not\equiv 0$ is converted to; considering, of course, that the conditions $k + 1 = m$ and $|a_k| = |b_m|$ are hold.

1) Having applied Property 1 with $b = 0$, $a = a$ to $p(z, \bar{z})$, we'll infer:

$$C(p(z, \bar{z}), \infty) = C(p(az, a\bar{z}), \infty);$$

supposing further that $a = \sqrt{\dfrac{a_k}{b_{k+1}}}$

(we'll mean any of its two values by the radical), and then applying Property 3 we infer:

$$C(p(z, \bar{z}), \infty) = a^{k+1} b_{k+1} C(p_1(z, \bar{z}), \infty), \text{ where}$$

$$p_1(z, \bar{z}) = (z^k + a_{k-1}^{(1)} z^{k-1} + \ldots + a_0^{(1)})\bar{z} + (z^{k+1} + b_k^{(1)} z^k + \ldots + b_1^{(1)} z + b_0^{(1)}).$$

Applying Properties 2 and 5 to $p_1(z, \bar{z})$ we infer:

$$C(p_1(z, \bar{z}), \infty) = C(z^k \bar{z} + z^{k+1} + b_k^{(2)} z^k + \ldots + b_1^{(2)} z + b_0^{(2)}, \infty),$$

where $z^{k+1} + b_k^{(2)} z^k + \ldots + b_1^{(2)} z + b_0^{(2)}$ is an integral part of a rational function

$$\frac{z^{k+1} + b_k^{(1)} z^k + \ldots + b_1^{(1)} z + b_0^{(1)}}{z^k + a_{k-1}^{(1)} z^{k-1} + \ldots + a_0^{(1)}} z^k.$$

If $k = 0$, then we get immediately that

$$C(a_0\overline{z} + b_1 z + b_0, \infty) = \sqrt{\frac{a_0}{b_1}} b_1 C(z + \overline{z}, \infty) + b_0 = \left\{ \sqrt{a_0 b_1} \cdot t + b_0 \mid t \in \overline{R} \right\},$$

and all the sequences (z_n) generating all finite points from $C(p(z, \overline{z}), \infty)$ are of the following form:

$$(z_n) = \left((x_n + iy_n) \sqrt{\frac{a_0}{b_1}} \right),$$

where (x_n) and (y_n) are arbitrary real-valued sequences possessing the property:

$$x_n \to \frac{t}{2} \in R, \text{ and } y_n \to \infty.$$

2) Denoting $p_2(z, \overline{z}) = z^k \overline{z} + z^{k+1} + b_k^{(2)} z^k + \ldots + b_1^{(2)} z + b_0^{(2)}$ $(k \geq 1)$ and passing on to real variables x and y, we infer

$$C(p_2(z, \overline{z}), \infty) = C\left(p_2(x + iy, x - iy), \left(-\frac{b_k^{(2)}}{2}, \infty \right) \right),$$

because (see Lemma 2) the coefficient $b_k^{(2)}$ can be thought as a real number (if not - $C(p(z, \overline{z}), \infty) = \{\infty\}$).

3) Having substituted the variables $x_1 = x + \dfrac{b_k^{(2)}}{2}$, we'll infer

$$C(p_2(z, \overline{z}), \infty) = C\left(p_2\left(x_1 - \frac{b_k^{(2)}}{2} + iy, x_1 - \frac{b_k^{(2)}}{2} - iy \right)(0, \infty) \right)$$

and having applied not more than $k - 1$ times Property 8 [5, 10], we'll "delete" all the monomials containing x_1 symbol (in the corresponding true degree), excluding $x_1 y^k$, and we'll get that

$$C(p_2(z, \overline{z}), \infty) = 2i^k C(x_1 y^k + p(y), (0, \infty)).$$

4) Dividing the real and imaginary parts of the polynomial

$p(y) = P_1(y) + iP_2(y)$, where

$P_1(y), P_2(y) \in R[y]$

(besides, on its proper inception $\deg P_1(y) < k$), we infer the following theorem [see 10]:

Theorem 2

Let $p(z, \overline{z})$ be a nontrivial polynomial of the form (3). Then $C(p(z, \overline{z}), \infty)$ has finite elements when and only when $p_2 = P_2(y) \equiv const$, in addition

$$C(p(z, \overline{z}), \infty) = \left\{ 2i^k \left(\sqrt{\frac{a_k}{b_{k+1}}} \right)^{k+1} \cdot b_{k+1} \cdot (t + ip_2) \Big| t \in \overline{R} \right\};$$

besides, all the sequences generating all finite points from $C(p(z, \overline{z}), \infty)$, are given by the following formula:

$$(z_n) = (x_n + iy_n) = \left(\left(\frac{t_n - P_1(y_n)}{y_n^k} - \frac{b_k^{(2)}}{2} + iy_n \right) \sqrt{\frac{a_k}{b_{k+1}}} \right),$$

where (t_n), (y_n) are arbitrary real-valued sequences, and also (t_n) converges to the finite limit t, and (y_n) - to ∞.

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PROJECTING COURSE IN MATHEMATICS ON THE IDEA OF INTERSUBJECT COMMUNICATIONS' GENERALIZATION

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In new social and economical conditions Higher School teachers face the necessity of specialists' training improving on the basis of integral combination of professional education with the high level of their fundamental training.

Mathematical Education in a Higher Technical School has the development of cognitive abilities at such a level of acquirement which could provide conscious using methods of routine problems' solution and research, their translation onto a non-routine problem (the problem with technical-grade content), i.e. on the level of conscious translation of mental activity approaches onto training objects of engineering disciplines, onto techniques and technology which will be used in the future work activity, as one of its basic aims.

The analysis of mathematical content of general professional disciplines shows that the definition of interactions between all courses of the curriculum of a Higher School represents a complex enough task. First of all, let us answer the question: Is it worth performing interactions between all the disciplines of the curriculum in equal amount? The absence of a clear answer to the question on practice leads to the fact that there is often a tendency to establish connections between all the disciplines of the curriculum of a Higher School in equal amount.

A specially carried out research and study of advanced pedagogical experience showed that

intersubject communications should have a certain didactic polarity that is to find out between which disciplines or their complexes on a certain speciality the connections are the most significant and cardinal, by means of a deep pedagogical analysis of the content of this speciality students' training. For the "Technology of Machine Building" speciality of the Samara State Technical University in Syzran they turned out to be the four complex programs: social and humane; economic and managerial; fundamental; general professional and special.

It is the elaboration and arrangement of conditions which are favourable for establishing connections between these general complex programs that should attract the efforts of the teachers by all means.

The experiment showed that it is reasonable to accentuate a frame discipline in every of the complexes penetrating all its components. So, Mathematics is such a discipline in the fundamental training; Technology of Machine Building is that in the professional one (on the engineer-mechanic's speciality); Branch Economics – in the economic and managerial one; philosophy – in the social and humane one.

Due to such an approach expressed in the generalization of intersubject communications, we manage to get rid of the necessity to elaborate very often not significant connections between any two pairs of the curriculum disciplines and to focus the greater deal of attention on the four mentioned complex programs reflecting the most cardinal connections between the frame disciplines of the curriculum.

Accentuating a group of disciplines the communications between which are the most significant, allows solving problems on curriculum perfecting, on topical and chronological integration of related courses' programs, on elaborating forms, approaches and methods of performing professional polarity of teaching fundamental disciplines rather definitely and purposefully

ANALYSIS OF ROTATION ACCURACY OF HIGH-SPEED SPINDLES WITH GAS-LUBRICATED BEARINGS

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The article presents a description of a test bench for analysis of rotational accuracy of a shaft supported by gas static bearings with partly porous shell walls and by those with orifice restrictors, along with the results of an experimental investigation.

High-speed machining is one of the leading directions in the development of modern manufacturing engineering. Introducing it in the metal-working industry allows to increase the productivity of labour along with the simultaneous improvement of machining accuracy and machined surface quality.

An important factor for successful realization of high-speed machining is the type of bearings used in spindle units (SU) of metal-working machines.

The work of spindle units supported by rolling bearings is accompanied, in particular, by an unstable spindle motion and thermal misalignment of bearing assemblies. Using hydrostatic bearings in high-speed spindle units leads to a spindle speed limitation (because of friction loss) and makes the design of the bearing assembly more complicated. Spindles supported by electromagnetic-bearings are not widely used so far because of their complication and the high cost of spindles and electronic control systems. Spindle units supported by gas-lubricated bearings are free of the above-listed shortcomings.

Gas bearings are reliable in operation both at high and low temperatures and humidity, the usage of them excludes pollution of the environment, reduces noise and vibration levels. Bearings of this kind are practically devoid of wear, that is why the high indices of spindle rotation accuracy remain invariable practically throughout the whole service life of machines.

Gas bearings have also some disadvantages which are in a comparatively low stiffness, bearing and damping capacities of the lubricant film. That is why bearings of this kind are used in light-loaded spindle units where the dynamic loads are light and the static loads are regulated.

The different problems of development and investigation of high-speed spindles with gas-lubricated bearings have been covered in a number of works [1–3] and others. In all presented designs of spindle units gas bearings with orifice flow restrictors were used.

At the same time, the analysis of externally pressurized gas bearings shows that it is precisely partly porous gas static bearings [4] that excel in the best operating characteristics (such as stiffness and bearing capacity of lubricant film). One of the designs of this kind of bearings – a double-row bearing with porous cylindrical inserts uniformly arranged in a pressurizing row – is shown in Figure 1.
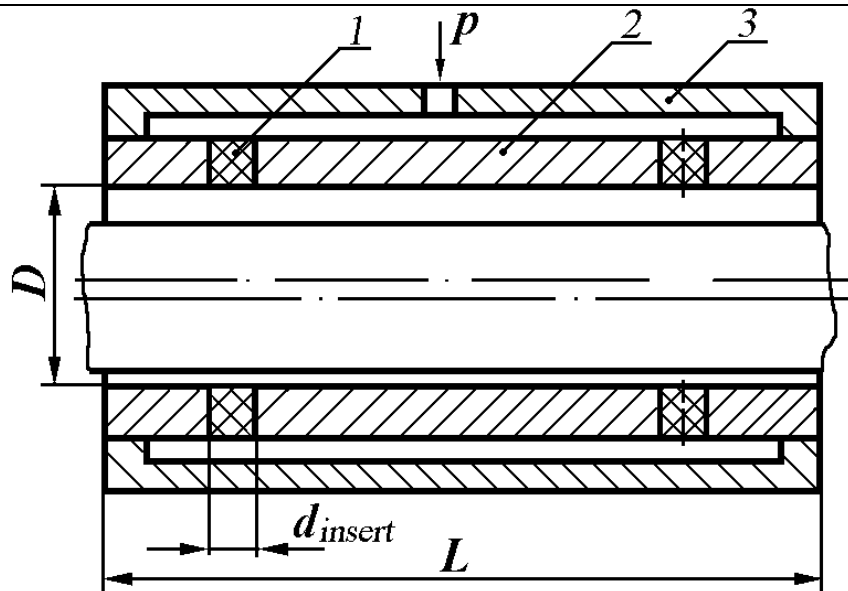
Figure 1. Partly porous gas static bearing:
1 – porous cylindrical insert, 2 – gas-tight bearing shell, 3 – bearing body

The work under review supplements the investigations [4] with experimental data on rotation accuracy of spindles supported by partly porous bearings and spindles supported by gas static bearings with orifice flow restrictors traditionally used in the metal-working-industry-used designs of high-speed spindle units.

The complex of experiments was carried out on a test bench which is represented schematically in Figure 2.
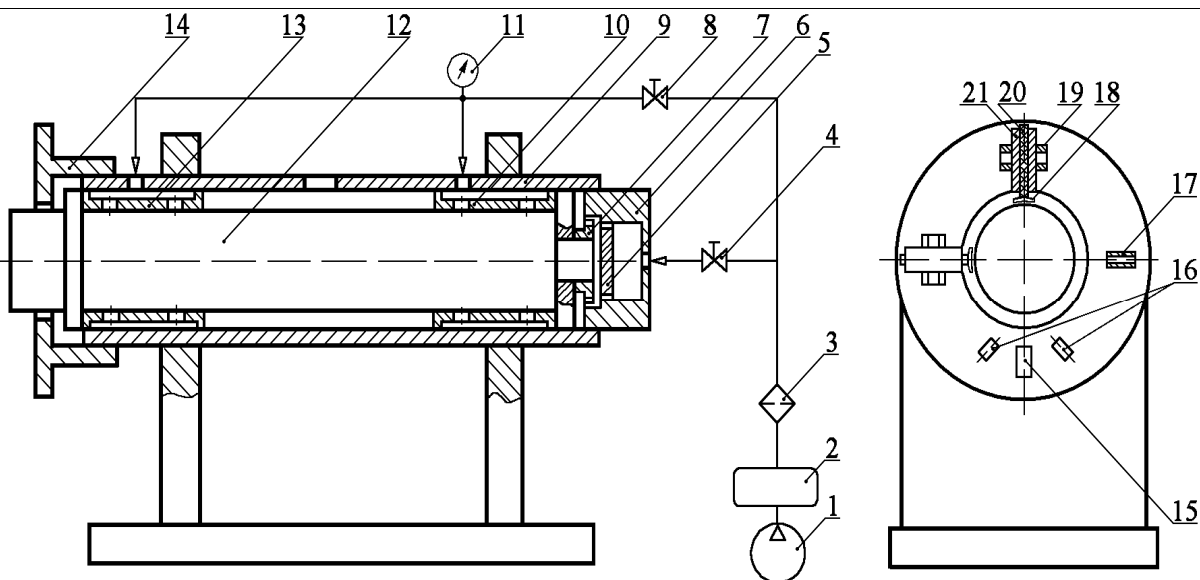
Figure 2. Diagram of the experimental test bench for the investigation
of shaft rotation accuracy

The main structural members of the test bench are shaft *12*, front *13* and rear *10* gas static bearings mounted in body *9*, turbine wheel *7*, nozzle diaphragm *5* secured in casing *6*, shield *14*.

The shaft was made of steel 30ХГСА (grade in accordance with GOST), its diameter was 50 mm and the length was 270 mm. The shaft surface was chromium-plated to a depth of 1 mm and hardened to the *HRC* 60-65 hardness. Once hardened, the shaft surface was finished to Class 10 with the surface finish $R_a = 0.16 \, \mu m$.

The double-row gas static bearings with porous inserts and those with supply holes were of the same geometrical dimensions (60 mm in length and 50 mm in diameter) and had an average radial clearance of 25 μm. The absolute gas boost pressure in the lubricant film was 0.3 MPa, which ensured equal values of the bearing supply parameter $\overline{m} = 7.2$. The distance between the centers of bearings was 170 mm. In each pressurizing row of the partly porous bearings there were six cylindrical porous inserts 8 mm in diameter. The air pressurization in the clearances of bearings with orifice flow restrictors was performed through two double rows of feeders. In each row there were 16 holes 0.5 μm in diameter.

The dynamic state of the shaft was determined by two capacitive transducers *20* with an area of 3 cm^2 each, placed adjacent to the shaft cantilever, one of them being mounted in a vertical plane and the other in a horizontal plane.

The shield was secured by screw joints at the butt-end of casing *9* in such a way that cover *18* of one transducer was arranged in a strictly vertical plane and that of the other one in a horizontal plane. The exact position of each cover with reference to the shaft center was achieved by moving slider *21* along guide *19*.

The transducers working surfaces were lapped to the shaft by a fine-grain diamond grinding emery paper. The lapping was carried out at a shaft speed of 360 min^{-1}. The emery paper was of about the same thickness that the working clearance of the transducer was (0.16…0.18 mm). To avoid an influence of the shaft journal errors (under the transducers) on the results of the experiment and for reliable work of optocouple *16*, the shaft journal has been previously lapped. The transducers position was checked by the УС 1-300 builder's level arranged at the guide of the vertically mounted transducer.

The sliders` guides and racks of micrometric indicators *15* and *17* are an integrated part of the shield. Their axes of symmetry form a right angle between each other. The calibration test of recorders` readings was executed with dial indicators graduated in 1μm. The results of the calibration test indicated amplitude linearity of the capacitive transducers.

The experimental test bench works as follows. The compressed air from compressor *1* passes through receiver *2* and filter *3* and arrives at the front and rear gas bearings of the shaft at a time; valve *8* adjusts air boost pressure in the lubricant film of the bearing. This pressure is indicated by standard pressure gauge *11.* When the shaft "floats up", valve *4* opens and the compressed air is delivered to the turbine stage. The shaft rotational speed was varied by flow action through the change of the rate of valve *4* opening.

The complex of experiments was carried out with the use of an automated investigating system which allows to solve the following tasks: to determine shaft speed, to measure rotating shaft motion in a lubricant film of bearings, and to build a shaft axis mechanical trajectory. The system was created on the base of a personal computer.

Electric signals from the transducer unit were fed to the original interface board for the ISA bus of the computer. The assembly program entered and processed measuring signals, stored results and displayed them in digital and graphic forms.

For shaft speed transducers we used a transistor infrared optocouple with open optical channel. The CQW58A-1 infrared diode and the Philips OP 500 phototransistor were arranged at an angle close to the shaft surface so that the light reflected from the shaft could hit the phototransistor. A black mark was made anywhere on the shaft to absorb the light flow. The interruption of the reflected light beam by the black mark during shaft rotating was used for measuring shaft speed and as a reference for determining shaft orientation from the angle of rotation.

The optocouple digital output signal came to one of three frequency inputs of the interface board. Through a program-controlled digital multiplexer the transducer signals were fed to the input of the impulse frequency meter mounted on the interface board. The frequency meter operating conditions were program-tuned, which provided an adequate accuracy of measurements of an input signal frequency in a wide range.

The measurement results were recorded in a file and then displayed on a monitor. The device-control and result-processing program set a graphic display mode. Orthogonal axes with scale marks were plotted on the monitor. The position of static shaft axis has been taken as the origin of coordinates. Thereupon reference points of the shaft motion in two coordinates were marked. The points were built at 5 degree intervals of the shaft rotation angle. The position of points between the measured points was established by interpolation with the use of Lagrange polynomial built on the data of four reference points nearest to each other. The shaft axis mechanical trajectory was built by joining adjacent points with segments.

The work of the horizontal and vertical shaft mechanical motion capacitive transducers was based on the principle described in work [4]. But there was a difference in using them which was in the way of processing signals coming from these transducers: the output signal was recorded only from one inverter input and, besides, an informational parameter in investigating the shaft rotation accuracy was not the relative rectangular pulse duration but the rectangular pulse frequency.

The mechanical motion transducers outputs were connected to two frequency inputs of the interface board. The frequency of signals coming from the outputs of the mechanical motion transducers was measured by the frequency meter. A transducer to be connected to the frequency meter was selected by a digital multiplexer.

Direct interrogation of the shaft speed transducer, without using the frequency meter, allowed the program to record the moment of passing through the black mark and to relate the shaft axis motion values being measured to this moment.

During the experiment the shaft rotational speed was changed from 12700 min^{-1} to 25400 min^{-1} which was appropriate to the variation of shaft specific speed $d\acute{}\,n = (0.63\ldots1.27)\cdot10^6$ mm/min.

The synchronous vortex paths of the shaft operated in gas static bearings with porous inserts (1) and with supply holes (2) at a specific speed of $1.27\cdot10^6$ mm/min are presented in Figure 3.
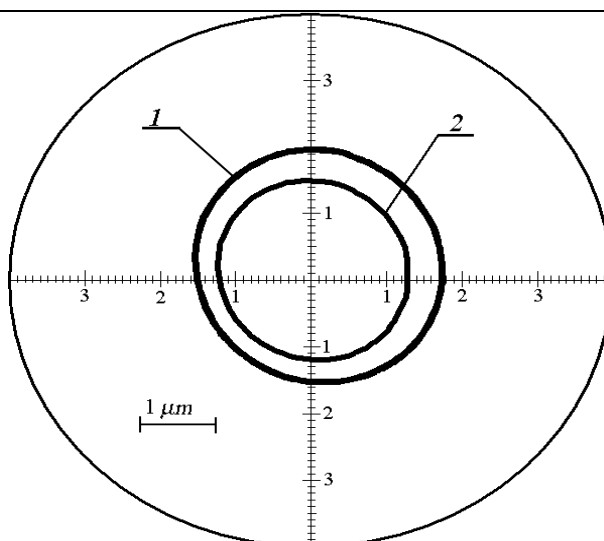
Figure 3. Synchronous vortex paths of the shaft in bearings
with supply holes (1) and with porous inserts (2)

The qualitative analysis of the synchronous vortex paths discloses their elliptic shapes which can be explained by variable stiffness of the lubricant film around the bearings. The path curves are smooth and practically not blurred, that is, the shaft axis moves in a constant trajectory taking up stable state in the bearings. The quantitative estimation of the experiment results shows a distinctly lesser radial run-out of the shaft supported in bearings with porous inserts.

The radial run-out considerably decreases as the shaft specific speed is reduced (Figure 4). In this case, the synchronous vortex path tends to assume the form of circle.
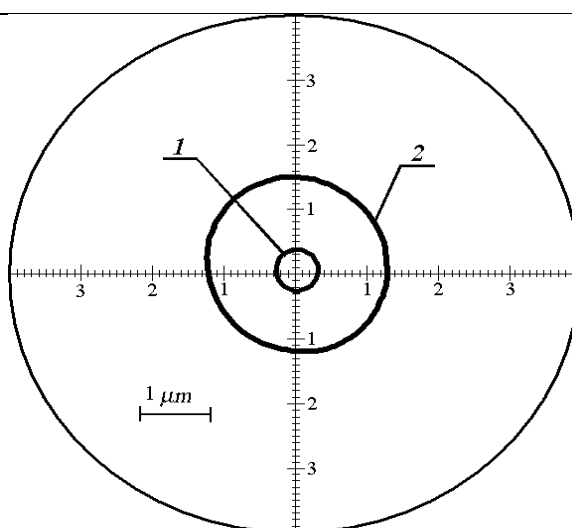
Figure 4. Synchronous vortex path of the shaft in bearings with porous inserts at a specific
speed of $0.63 \cdot 10^6$ mm/min (1) and $1.27 \cdot 10^6$ mm/min (2)

The synchronous vortex paths presented in Figures 3 and 4 were registered in 300 revolutions of the shaft. In the course of the experiment the shaft trend, that is to say, a variation in time of an expectation value of the set of paths [5], has not been noted, which indicates that the bearing heat release was not essential.

The results of the performed complex of investigations into rotation accuracy of the shaft supported by gas static bearings with porous inserts and of the shaft supported in bearings with supply holes are shown in Figure 5.
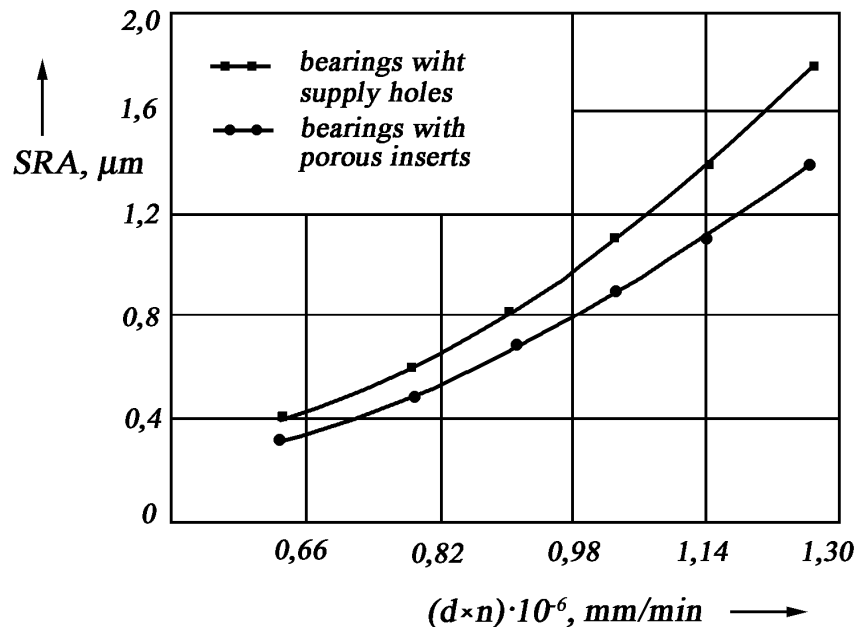
Figure 5. Dependence of the shaft rotation accuracy (SRA) upon the specific speed $d \times n$

From the dependences presented here it is clear that throughout the covered range of shaft specific speed changes the radial run-out in bearings with porous inserts is less than it is in bearings with supply holes. As calculated, the decrease of radial run-out of the shaft is 16…22%.

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HIGH-SPEED GRINDING MACHINES WITH TURBINE DRIVES AND GAS-LUBRICATED SPINDLE UNITS

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The article presents designs of air grinding tools with gas-lubricated bearings and turbine drives as well as their technical characteristics.

In industry a great amount of works is carried out with the use of air grinding tools.

The air grinding tools offered on the market by Russian and foreign companies are, for the most part, low-speed ones with a volumetric rotor motor which have a great specific weight per unit of power. As a result of the rotor unbalance and using rolling bearings in this kind of air tools, substantial noise and vibration levels occur. The operating life of the bearings themselves is not long.

Nowadays, abrasive disks with a peripheral velocity of up to 120 m/sec are commercially produced. To use them more effectively, a high-speed air tool capable to provide increased productivity became a necessity. This requirement is met by air turbine grinding tools with gas-lubricated bearings.

The use of gas bearings allows to reduce abrasive and milling tool wear, to extend considerably air tool service life and to increase productivity at low cutting forces, to solve the problem of an operator protection from vibration and acoustic actions, to improve work-piece surface finish, to ensure reliable work in dusty places as well as at high and low temperatures and humidity.

There is a number of designs of air grinding tools with gas-lubricated bearings presented in technical literature [1-3]. But for various reasons, this kind of tools is not so far commercially produced in Russia. They are entirely absent in the ranges of products of leading foreign companies in the field of air grinding tools (Atlas Copco, Dezoutter, Bosch, etc.).

It is apparent that the widespread introduction of air grinding tools with gas-lubricated bearings into the industry should be quickened by the works on the improvement of tool designs which provide low-cost production practice in enterprises with up-to-date machinery. Special attention should be paid to the commercial design of tools, their unit and component materials.

The solution to the problem has been embodied to an extent in three designs of the high-speed air grinding tool Models ВПМШ 150.01, ВПМШ 035.01 and ВПМШ 015.01 developed at the Komsomolsk-on-Amur State Technical University (KnASTU).

The general view of the high-speed air grinding tool Model ВПМШ 150.01 is shown in Figure 1.
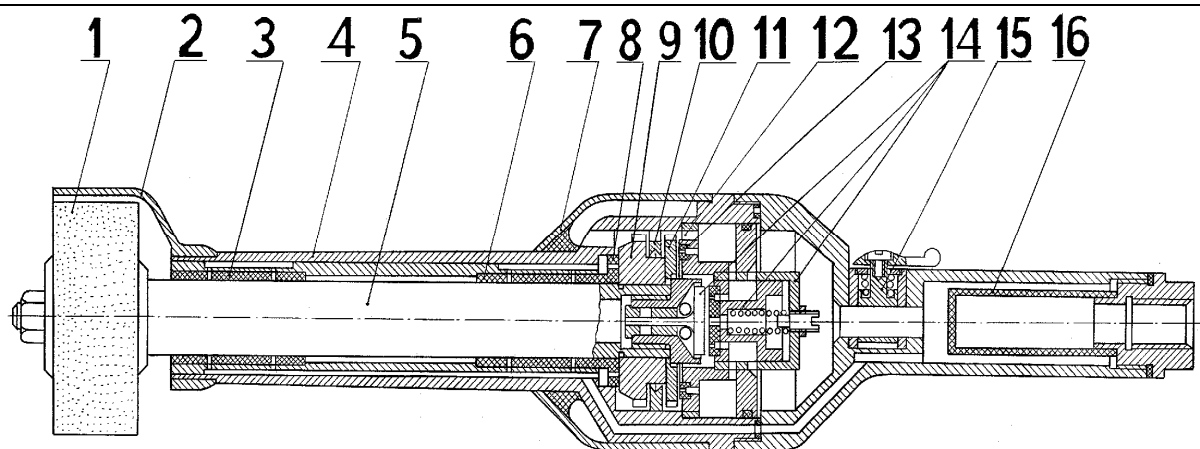
Figure 1. Design of the air grinding tool Mod. ВПМШ 150.01

The tool is dedicated for edge preparation, weld finish, foundation surface finish, etc. The main structural members of the Mod. ВПМШ 150. 01 are a body, a spindle, a turbine drive, gas static bearings, a rotational speed governor, a noise silencer, an air filter and a starting valve.

Tool body *4* is made of aluminum alloy and anodized (the coating thickness is 10…20 μm). There are some drill holes in the body for supplying compressed air to and removing from the gas bearings. Ahead, on the thickened part of the body there is an outlet for the turbine-used air.

For the accurate conjunction of components, the internal surfaces of the body have been finished to R_a = 0.32 μm at a radial run-out of no more than 10 μm.

Spindle *5* is made of steel 30ХГСА (grade in accordance with GOST), heat-treated to *HRC* 45…50 and chromium-plated. The high surface hardness and finish achieved by grinding lessen the probability of spindle damage in case of accidental contacts or abrasive particles fallen into the clearance. To reduce unbalance, axial spindle run-out of no more than 5 μm is permissible.

Grinding wheel *1* or a milling cutter is attached to the output end of the spindle by a collet chuck. At the opposite end of the spindle there is a groove for attaching first-stage turbine wheel *11* and second-stage turbine wheel *9*. Between the turbine wheels there are guide vanes *10* and ahead of the first-stage wheel is nozzle diaphragm *12* with converging nozzles. The small-sized turbine is a double-row one with velocity stages. The outer diameter of the turbine drive wheels is about 75 mm. As the turbine disks material, we use duralumin Д16Т. Using a light alloy for this purpose reduces the unbalance and stress levels in the disks and blade root section which occur by the action of centrifugal forces.

The turbine wheels have shrouds which reduce channel-to-channel air leak along the blade end surfaces and through the radial clearance.

The high-speed air grinding tool Mod. ВПМШ 150.01 is fitted with two gas journal bearings and two gas thrust bearings. Journal bearings *3* and *6* with drain grooves are double-row ones with 12 holes 0.4 μm in diameter in each row. The relative length of the bearings is 1.2. For the maximum load-bearing capacity the clearance between spindle and bearing shells is 50…70 μm. One journal bearing can endure a load of about 60 N at the relative eccentricity *e* = 0.5.

The axial force is taken by bearing *8,* with the second-wheel disk as its thrust collar, and by end thrust bearing *13* of

rotational speed governor *14*. The thrust bearing faces are provided with labyrinth seals. The bearings have 12 supply holes each, these holes being placed in two annular rows. The diameter of each hole is 0.4 mm. One thrust bearing can endure a load of about 50 N.

The shells of both journal and thrust bearings are secured in mounting seats by pasting-in. For this purpose epoxy-resin adhesive is used. As the practice has shown, this kind of joint is reliable in operation and easy to perform.

The bearing-shell material is black-lead АГ1500 Б83. It has low friction coefficient and does not "catch hold" with the metal in case of accidental contacts at high speeds. Black-lead also behaves well in humid gases.

To reduce high-frequency noise generated by the turbine, the tool is provided with silencer *7*. The principle of its operation is in reducing the flow energy owing to its repeated turns and expansion. The noise silencer presents a cap screwed on to the turbine casing.

For removing solid particles and oil from the air, the tool is fitted with filter *16* made of porous material. The choice of material was defined by its low resistance to air flow and capability to pass particles which are smaller in size than the average radial bearing clearance, which makes it possible to remove particles from the clearance with the air flow.

Casing *2* protects an operator from chips, abrasive particles or a sudden break of an abrasive disk.

The air grinding tool Mod. ВПМШ 150.01 works as follows. When joining the tool in air mains and with starting valve *15* close, the compressed air is delivered to the journal bearings only, allowing the spindle "to float up". With the starting valve open, the air goes simultaneously to the thrust bearings and, through the nozzle diaphragm,

to the turbine wheels, making the spindle to rotate. The turbine-used air emerges through the opening, expands in the space between the silencer cap and the body and leaves the tool through the drilled holes in the cap.

The designs of air grinding tool Mod. ВПМШ 035.01 and ВПМШ 015.01 presented in Figure 2 differ from the Mod. ВПМШ 150.01 in that they have no speed governor and turbine wheel shroud. The nozzle diaphragm is combined with the thrust bearing. Besides, the drive of the Model ВПМШ 015.01 is a simple-impulse turbine.

As a material for the gas-bearing shells in the Models ВПМШ 035.01 and ВПМШ 015.01 we use bronze black-lead. The shells are made by the powder metallurgy method. This material is more workable than black-lead. Bronze black-lead has low friction coefficient and, along with black-lead, behaves well in humid air. The steel-bronze combination does not produce strong adhesive bonds between each other which can cause spindle failures such as deep tears and stretches.

Owing to "self-balancing" of the grinding wheels during the operation, all the tools run steadily at a rated rotational speed till the full wear of grinding wheels. In the design of a turbine drive for the presented here air grinding tool models, we used the latest scientific achievements in the field of experimental study of small-sized turbines, with updating the mathematical model as applied to the object to be developed. The journal and thrust gas static bearings were designed in accordance with the KnASTU developed method of performance calculations [4]. As a whole, the design calculations of a turbine drive and gas bearings are oriented to the modern engineering capacities of Russian enterprises.

The technical characteristics of the developed air tools at a compressed air pressure of 0.5 MPa are presented in Table 1
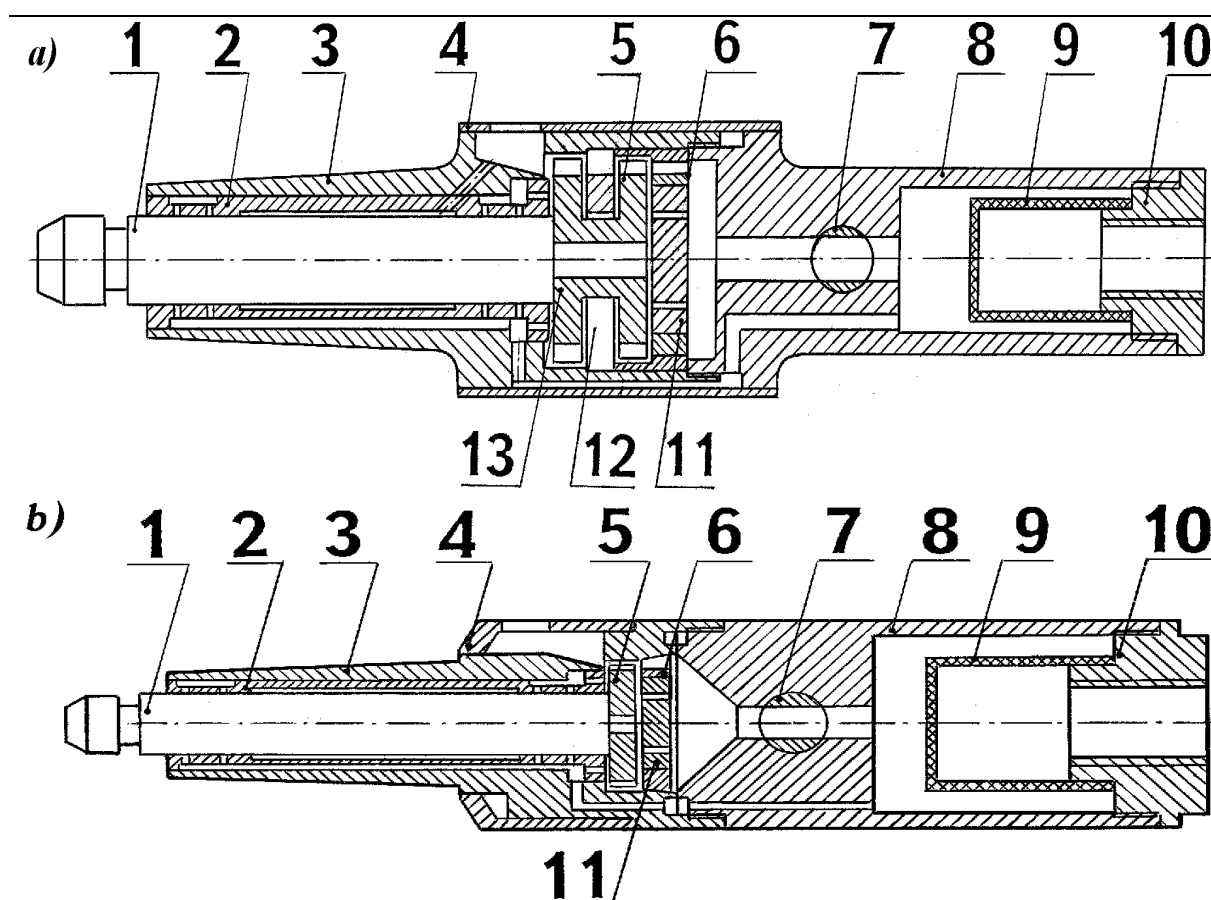
Figure 2. Designs of the high-speed air grinding tool
Mod. ВПМШ 035.01 (*a*) and ВПМШ 015.01 (*b*):
1 – spindle, 2 – gas static journal bearing, 3 – spindle body, 4 – silencer, 5 – first-stage turbine wheel, 6 – nozzle diaphragm, 7 – starting valve, 8 – turbine casing, 9 – filter, 10 – nipple, 11 – thrust bearing, 12 – guide vanes, 13 – second-stage turbine wheel

Table 1. The technical characteristics of the developed air tools at a compressed air pressure of 0.5 MPa

Characteristic	Model		
	ВПМШ 150.01	ВПМШ 035.01	ВПМШ 015.01
Drive power, kWt	1.5	0.25	0.085
No-load spindle speed, rpm	29000	105000	237000
Air consumption, m^3/min	1.90	0.68	0.29
Overall dimensions, (L x W), mm	380 ´ 83	260 ´ 48	175 ´ 33
Weight, kg	3.60	0.65	0.25
Collet chuck diameter, mm	10	6	6
Specific speed (spindle diameter ´ rotational speed), mm/min	$5.5 \cdot 10^5$	$1.47 \cdot 10^6$	$2.13 \cdot 10^6$

With 120 m/sec abrasive machining speed, it is acceptable to fit the air grinding tool Models ВПМШ 150.01, ВПМШ 035.01 and ВПМШ 015.01 with grinding wheels

accordingly 80, 20 and 10 mm in diameter. Such relatively small diameter values are not limiting ones, because even at present a number of enterprises are ready to produce abrasive wheels running at rim speeds up to 300 m/sec.

The air tools beta tests were carried out by PC "KamAZ-Instrument", the Irkutsk Research Institute of Aircraft Technology and Industrial Engineering, JSC "Amur Ship-building Plant" and the Komsomolsk-on-Amur Aircraft Production Association named after Yu.A. Gagarin. Their expert commissions have pointed out a steady work of the tools over the whole load range, a higher productivity (3-5 times higher) in comparison with the industry-used tools, high surface finish ($R_a = 0.63…1.25$ µm when milling copper or aluminum alloys, and $R_a = 0.16…0.32$ µm when machining steels with the use of spray coolants), smooth startup and no vibration notable for an operator.

The measurement of noise and vibration levels of the air grinding tool Models ВПМШ 035.01 and ВПМШ 015.01 was performed by the State Hand-Held Machine Testing Center and those of the Model ВПМШ 150.01 was performed by Dalzavod (Vladivostok). The actual sound power levels of the air tools are shown in Figure 3.
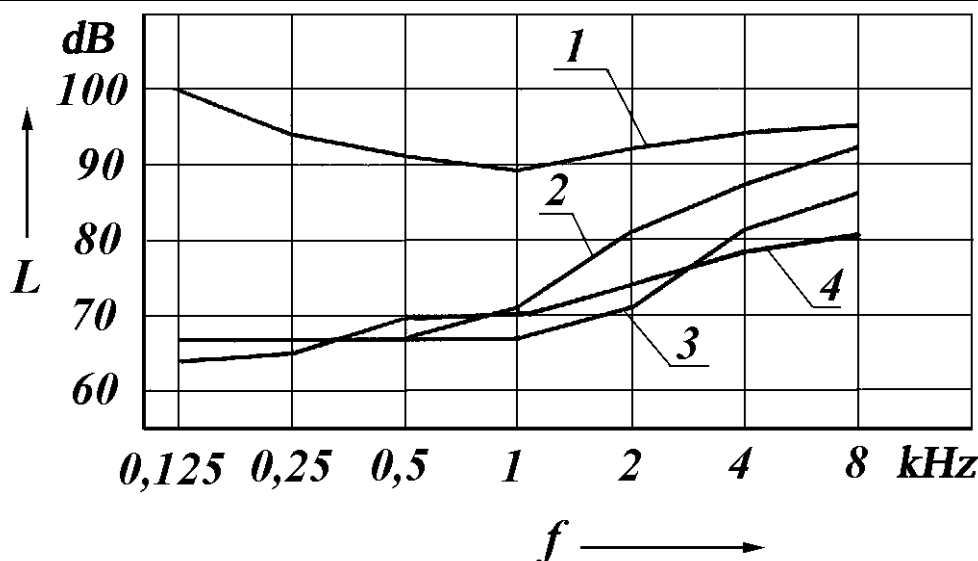
Figure 3. Actual sound power levels *L* of the air grinding tools in center frequencies octaves-bands *f*:
1 – GOST 12.2.030-83, 2 – ВПМШ 035.01, 3 – ВПМШ 015.01, 4 – ВПМШ 150.01

The results of the air tool vibration level tests are presented in Table 2 where first is the parameter of the Mod. ВПМШ 150.01, next is that of the Mod. ВПМШ 035.01 and last is that of the ВПМШ 015.01.

According to GOST 17770-86 "Hand-held machines. Vibration characteristics requirements", the permissible vibration level on all center frequencies is 109 dB.

Table 2. The results of the air tool vibration level tests. First the parameter of the Mod. ВПМШ 150.01, next is that of the Mod. ВПМШ 035.01 and last is that of the ВПМШ 015.01.

Direction	Vibration level (dB) at center frequency (Hz)							
	8	16	31.5	63	125	250	500	1000
X	60/94/92	60/108/97	60/107/81	61/101/79	72/100/83	75/104/87	65/102/86	64/101/85
Y	58/93/99	61/109/104	62/108/88	59/107/80	60/105/80	78/99/80	66/100/81	61/104/82
Z	62/106/96	61/108/102	60/105/85	62/101/79	64/99/79	76/97/79	64/98/80	62/97/81

The air grinding tool Models ВПМШ 035.01 and ВПМШ 015.01were put into full-scale production in the amount of 1200 pcs/month by LC "Contact" (Komsomolsk-on-Amur). As a result of this tool testing, a hygiene certificate has been issued by the Russian Federation State Committee of Sanitary and Epidemiological Inspection.

The tools designs, their main structural members and units are covered by the Russian Federation patents. The developed air grinding tools are in demand in Russia, CIS countries, South Korea, China. The tools were also demonstrated at a number of Boing Corporation enterprises (USA).

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PARTLY POROUS GAS STATIC BEARINGS OF HIGH-SPEED SPINDLE UNITS OF METAL-WORKING MACHINES

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Operating characteristics comparison of gas static supports with porous and, widely used in speedy spindle industrial constructions, gas bearings with feeding holes is given. Construction and technical data of a high-speed unit on gas static supports with porous inserts are described.

One of the important problems of mechanical engineering is in achieving a high accuracy and parametric reliability of metal-working machines.

Already at a stage of design calculations, there is a need to develop such machine assemblies and elements which would be able to provide a specified accuracy of machining throughout their service life. The investigations [1] on estimating the influence of different factors on the accuracy of machining show that it is about 80% determined by a spindle unit. Since the shape-generating motion is carried out by a spindle and spindle bearings, it is precisely they that are of crucial importance in the output characteristics of machines.

The work of spindle units supported by rolling bearings is accompanied, in particular, by an unstable spindle motion and thermal misalignment of bearing assemblies. Using hydrostatic bearings in high-speed spindle units leads to a spindle speed limitation (because of friction loss) and makes the design of bearing assembly more complicated. Spindles supported by electromagnetic-bearings are not widely used so far because of their complication and the high cost of spindles and electronic control systems. Spindle units supported by gas-lubricated bearings are free of the above-listed shortcomings.

A long-standing experience of the Experimental Scientific Research Institute of Metal-Cutting Machines (ESRIMM) [2] in operating high-speed gas-bearing spindle units in conditions of small- and full-scale production has enabled to reveal their main advantages over the rolling-bearing spindle units, namely, longer lifetime determined by the time of spindle operation with a steady quality of grinding, better quality of grinded surface due to lower spindle sensitivity to the unbalance of a mandrel and wheel, no need to warm-up spindle, much lower (4 – 5 times lower) level of vibration, lesser wear of a grinding wheel.

Gas bearings have also some disadvantages which are in a comparatively low stiffness, bearing and damping capacities of the lubricant film. That is why bearings of this kind are used in light-loaded spindle units where the dynamic loads are light and the static loads are regulated.

The output characteristics of high-speed spindle units supported by gas-lubricated bearings can be significantly improved by using gas static bearings with a partly porous shell wall. Some results of the investigation into characteristics of this kind of bearings under radial load on the spindle are presented in Works [3, 4]. Meanwhile, the actual operation of a spindle unit is characterized by that the spindle reacts the radial load which leads to a displacement of the spindle centre

in the plane $X\,O\,\bar{z}$, simultaneously with the longitudinal moment causing a spindle axis displacement in the plane $X'\,O\,\bar{z}$ (Figure 1).
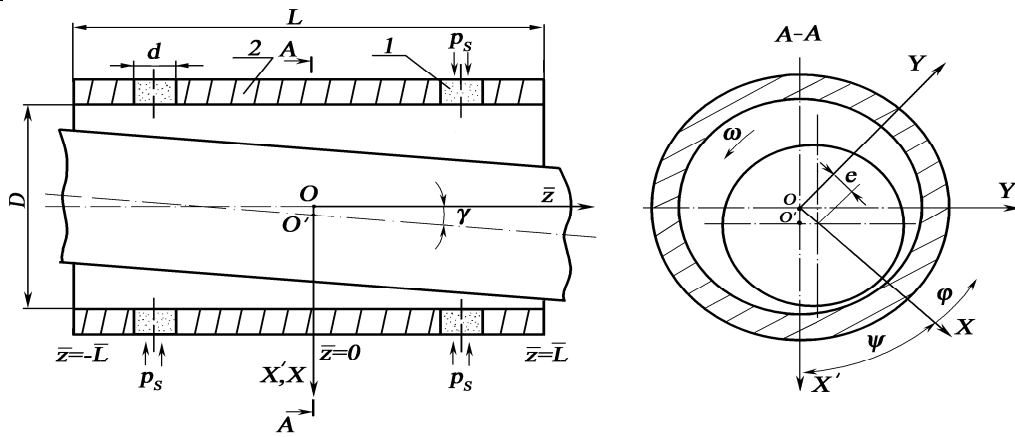
Figure 1. Diagram of spindle position in a double-row gas static bearing with porous inserts: 1 – porous insert, 2 – gas-tight surface of a shell

Taking this into account, there has been developed a procedure for calculation of operating characteristics of a partly porous gas static bearing with consideration for a spindle axis misalignment in the bearing shell. The procedure is based on a numerical method of calculation of the bearing

$$\bar{h} = h/c = 1 - e\cos j - (\bar{g}/\bar{L})\bar{z}\cos(j - y),$$

where c is the average radial clearance between the spindle and the shell, $e = e/c$ is the relative eccentricity, $\bar{g} = gL/(2c)$ is the misalignment parameter, $\bar{L} = L/D$ is the relative length of the bearing, j is the angular coordinate, y is the angle of load orientation, $\bar{z} = 2z/D$ is the relative axial coordinate of the bearing. The integration of Reynolds equation was made in the variation ranges of independent variables $-\bar{L} \le \bar{z} \le \bar{L}$ and $0 \le j \le 2p$.

The devised procedure has enabled to conduct a widespread theoretical investigation into the angular characteristics of gas bearings with porous inserts and to compare them with the characteristics of gas static bearings with supply holes (restrictors) which are usually used in the industry-used

characteristics at only radial load on the spindle and is detailed in Work [4]. Without going into details of the developed procedure, it should be noted that the relative clearance between the spindle and the shell was given by the following formula:

designs of high-speed spindle units. This comparison was made at equal values of non-dimensional parameters of bearings – the parameter of regime $\bar{m}$, the relative length of bearings $\bar{L}$, the relative gas boost pressure $\bar{p}_S = p_a / p_S$ and the value of compressibility B. So, for example, Figure 2 shows the dependence of the angular stiffness k_g upon the relative eccentricity e of the double-row gas static bearings with porous annular inserts and those with supply holes of a simple orifice type and annular type. From the shown dependences it is clear that, excluding the range of very low values of the relative eccentricity ($e < 0.2$), the partly porous gas static bearing has higher values of the angular stiffness.
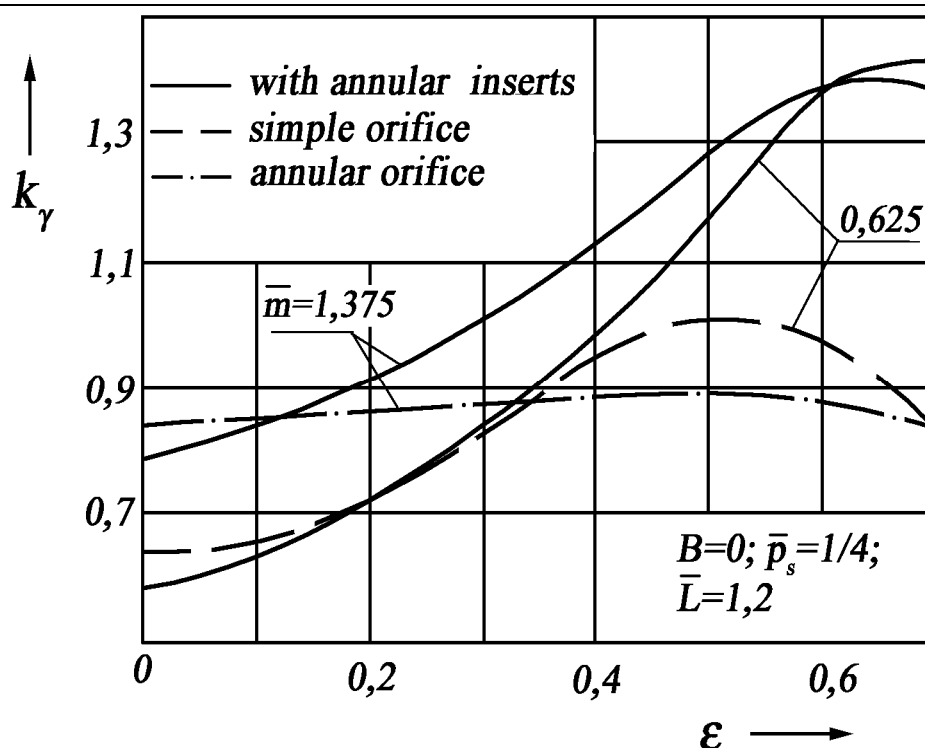
Figure 2. Comparison of characteristics of gas static bearings with annular inserts and those with supply holes in the angular stiffness k_g

As a whole, it was found by way of calculation that in the range of working values of the relative eccentricity ($e = 0.4 – 0.8$) the radial stiffness coefficient of partly porous bearings is 10–30% higher than that of spindle bearings with supply holes, the angular stiffness coefficient is 30–35% higher, and the coefficient of carrying capacity is 10–20% higher.

Additionally, a comparison of stiffness on a grinding wheel for a spindle supported by gas static bearings with porous inserts and those with supply holes was made by an example of their using in the commercial design of the electro spindle Model A24/25, the technical characteristics of which are described in Work [5]. It has been determined that with the spindle supported by the bearings with a partly porous shell wall the stiffness on its grinding wheel can be about 23% higher.

To check the correspondence of the theoretical results of the investigations with the actual data, a physical experiment has been carried out for estimating the influence of the shaft displacement y at the different relative gas boost pressure $\overline{p}$ on the load F measured on the shaft cantilever. The analysis of the obtained results showed in Figure 3 indicates that the error of theoretical determination of the load F on the shaft cantilever does not exceed 17% of the stiffness $k_F = F / y – 15\%$.
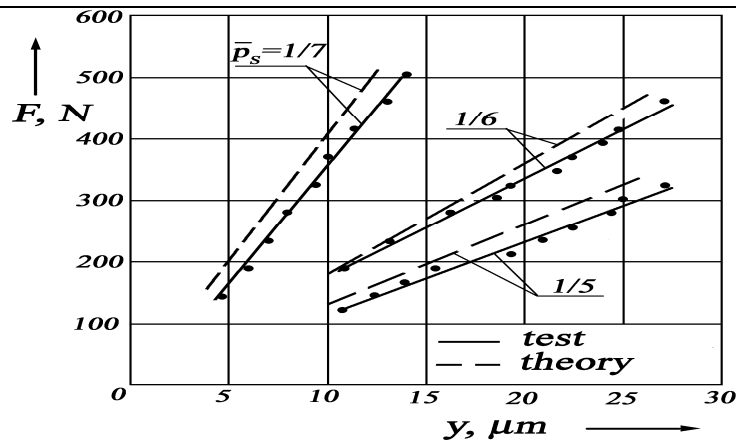
Figure 3. Dependence of the load *F* on the shaft cantilever upon the shaft axis displacement *y* and the relative pressure $\overline{p}_S$

The results of the investigation into operating characteristics of gas static bearings with a partly porous shell wall formed the basis for developing a high-speed spindle unit which was put into operation at the Komsomolsk-on-Amur branch of JSC "Sukhoi Design Bureau". The spindle unit is operated as a part of the grinding machine Model 3A228. Its design is shown in Figure 4.
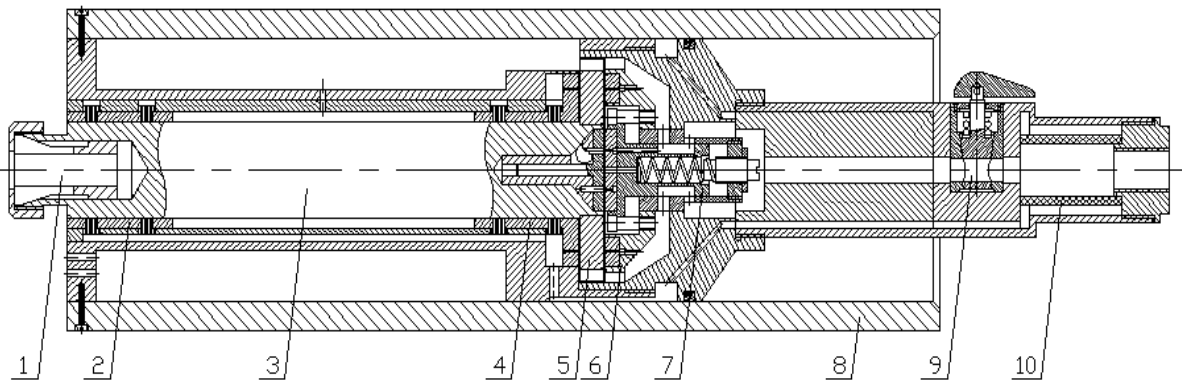
Figure 4. Design of the high-speed internal grinding spindle unit:
1 – collet chuck, 2 – journal bearing, 3 – spindle, 4 – journal-thrust bearing,
5 – turbine wheel, 6 – nozzle diaphragm, 7 – limiting rotational speed governor,
8 – sleeve, 9 –valve, 10 – filter

The gas bearings of the spindle are one double-sided thrust bearing with micro labyrinths and two radial bearings with partly porous shell walls. The radial bearings each have two rows of porous inserts 4 mm in diameter which are evenly situated over the circumference. The material of the inserts is porous bronze made by the method of powder metallurgy.

With a spindle diameter of 30 mm, the relative length of bearings is 1.2. The relative distance between the porous inserts and the bearing end surfaces is 0.26. The average radial clearance *c* is 17 μm. The bearing shells are of bronze Br010 (Бр010) and the spindle is of high-speed steel P18 (grade in accordance with GOST). Once been turned, the spindle was hardened to the *HRC* 60-62 hardness with cooling below 70 °C between

intermediate temperings. Such heat treatment stabilizes the structure of the metal and thereby prevents the spindle from warpage in the future. Once the spindle surface has been finished, the form deviations such as taper, out-of-roundness, barrelshapedness, etc., were no more than 10 μm.

At an excess air pressure of 0.5 MPa, the spindle unit has the following technical characteristics:

Power, kW…………………………………………………1.6
Rotational speed, rpm….. ……………………………….32000
Specific speed, mm/min……………………………………$9.6 \cdot 10^5$
Diameter of hole grinded, mm…………………………… max. 200
Diameter of grinding wheel, mm…………………………..max.70
Overall dimensions:
    sleeve diameter, mm…………………………………100
    length, mm……….…………………………………….400
Weight, kg…………………………………………………18

The testing of the prototype internal grinding spindle head carried out at the branch of JSC "Sukhoi Design Bureau" has shown a good quality of holes grinded by the 25CT18K electrocorundum wheel (steel X18H10T (grade with accordance to GOST), the roughness R_a does not exceed 0.04 μm), a high accuracy of machining them (the circularity deviation is no more than 0.2 μm, the surface undulation in lapping mode has not been found) and a trouble-free operation of the gas bearings. Also it was determined that, when using the developed spindle unit design, the wear of grinding wheel is 1.4 times less in comparison with the industry-used high-speed spindle head Mod. ВШГ 000.000РЭЭ supported by rolling bearings. The labour productivity in this case is 2.3 times higher.

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Materials of the Conferences

ACCURACY INCREASE AND SIMPLIFICATION OF PARALLEL ANALOG-TO-DIGITAL CODER MEANS

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The known at present time methods of "voltage-code" converting significantly differ from each other with the converting rate, hardware implementation difficulty and potential accuracy. Undoubted leaders in the first two categories appear analog-to-digital coders (ADC). Thanks to the simultaneous work of $2^n - 1$ equalized comparator units paralleled to the source of home signal, the base voltage of which is formed by 2^n resistors, the parallel ADC are the quickest. For example, one-of-eight decoder MAX 104 allows getting 1 billion indications per second.

But a disadvantage of a parallel ADC is a high complexity and, as the consequence of it, a high price (hundreds of US dollars) and a considerable power intake (about 4 W); the number of comparator units redoubling with the ADC code length (and it means its accuracy) increase. When the register length is more than 6-8 bits, the scheme becomes extremely bulky. This is what limits the use of parallel ADC in practice.

The research carried out by the authors showed that one of the most optimal ways of accuracy increase and simplification of parallel ADC means, which are used for bipolar signals conversion, can serve introducing a sense and negative voltage inversion unit, completing activity of sensing (the polarity) of home signal voltage, creation of voltage module of home signal and its following relaying with a unitary ratio of transmission, into the ADC composition scheme

Introducing the offered unit into the composition of one-of-n ADC means for analog-to-digital processing of bipolar signals and negative polarity signals is equal to:

a) output pattern increase by one digit on account of introducing an additional bit (the polarity sign code), and the ADC accuracy increase being meant by it without saying;

b) simplification of ADC means on account of negative voltage inversion, that will allow reducing ADC code length from n to (n-1), and it means - reducing the number of comparators twice as much;

c) reducing power consumption (in terms of one digit of a parallel ADC) practically twice as much on account of the means' simplification.

DEEP ELECTROCHEMICAL 2D BARCODE MARKING OF GOODS

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The international standard of quality system management ISO 9001:2000 requires carrying out the identification of each product in every technological cycle. Linear barcodes, which initially were considered to have high quality contrast and denotation, are put on a paper basis or on labels that can result in further loss of information. Such marking allows putting not more than 30 figures, that not always let code the necessary volume of information. All this has led to the appearance of bi-dimensional (2D) notation, which allows to code hundreds times more information; is meant for direct drawing on products; has greater information security due to compaction, duplication and the system of mistake correction of Read-Solomon.

The possibility of electronic sensing under any angle, the possibility to read at 20% contrast of marking signs relative to the surface (for a linear bar-code it is required not less than 80-90% of contrast) refer to the advantages of matrix marking, Data Matrix, for example; the possibility to dimensional scaling and distant reading are available. In a square marking sized some millimeters only, up to 2335 alphanumeric

signs can be put. Actually, it is a portable database.

One of effective conductive surfaces' marking methods is electrochemical marking (ECM). Typical installations of ECM use solid tool-electrodes (TE) and a data entry screen with hollows in the image of the picture being marked, there being no electrolytic flow canal; the process is carried out by means of electrolytic damping of a porous layer. It limits the marking depth. Besides, such screens allow to apply a limited number of markings, require special materials and printers or using photolithographic methods for stamping.

The installations having the minimized and equal interelectrode-gap gage (IEG), along the whole surface and providing the conditions for the uniform electrolytic flow allow actualizing the ECM advantages to the full extent. The useful area of the developed by us TE for ECM with matrix notation sized 10x10 elements is a flat die made by the ends of isolated copper conductors of 0,35 mm diameter which are disposed in the form of a rectangular screen. The IEG is 0,1-0,2 mm, the electrolyte being prepared on the basis of sodium chloride or sodium nitrate.

We also developed a method of TE units' commutations with photo-elements' use which doesn't contain mechanical circuit changers and without using complex programming devices. Every TE unit was connected with a photo-resistance on a flat panel through a reinforcing agent, and the disposition of the photo-resistances corresponding to every TE unit. The treatment was carried out by direct or alternate (for blackening) current. To do it a light image, in correspondence to which the commutation and current passage through TE units was carried out, was projected on the photo-elements' die through a light-sensitive film or a photomask on the photocell matrix. The signs' depth was 0,2 mm at the processing time of 40 sec., that is sufficiently higher than the mask methods of ECM.

Materials of the Conferences

TO A PARITY OF TRUE AND KNOWLEDGE OR WHY K. POPPER DEPRIVES THE SCIENCE OF ITS COGNITIVE CONTENT?

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The methodology of a science differs procedures: on the one hand, it is formal-logic profile, on the another it provides functions of dialectic logic in the knowledge. Both are successfully used in opening true, but are unequally effective in their substantiation and the proof. The formal-logic ways and principles are exhausted themselves basically in formation of true whereas realization of potential of dialectic logic leads cognition up to reception of knowledge. More often these processes do not synchronize: formation, formulation of true precedes its verification, only after which it is lawful to speak about knowledge. The substantiation of the validity of knowledge is carried out by the dialectic logic in close communication with practice which bounds not only criterial, but also creative operations of the subject of knowledge. However the place, time and results of the last in knowledge differs it from corresponding creative functions of methods and principles. Here, in our opinion, the dual role of criterion of true is the practice. The criterion of practice is ambiguous: it is uniform with methodological principles and possesses actually both heuristic and verifying functions

As an important reason this circumstance stands against wide popular beliefs about «uncertainty and an inefficiency» of practice as criterion of objectivity of the knowledge, more increasing declaring about itself and in domestic philosophy. For example I.Kasavin writes «The norm demanding of use of criterion of practice is nonfunctional when it is a question of world-wide-historical public practice and about distinction of materialism and idealism: it is not internally connected with the concept of true when the concrete knowledge and a concrete practice are meant. In the latter case more applicable are private methodological norms and

criteria of true…»[1]. The author of quoted clause supports such pluralism of criteria of true among which practical function is not allocated a special place.

The methods and the principles, carrying out its basic constructive function in cognitive creativity, are not fenced off, certainly, from correcting, verifying with the norms which have developed owing to practice of knowledge, procedures etc. Methodological principles can reveal effectively enough the conformity with valid denotes to any side of content or the form of true. Let's remember Cartesian "self-evidence", Leibniz's "non-contradiction", Kant's formal criterion and others. Being limited in this profile, we are not capable to measure the rich content of true's representant. The methods and principles even in dialectic set do not carry out a role of universal, objective criterion.

It is clear, the practice as criterion of true also is not certain "magic stick". Its relativity and limitation follows from concrete historical character of practice, consists in insufficiency of separate practical act and sometimes and the big number of acts for definition of the true or false representations; endless of positions and conclusions of practice takes place. Moreover, it is helpless in cases of temporarily or essentially not relative with the object of reflection of forms of knowledge. The subject of knowledge can be disoriented due to erroneous representations. But it sometimes leads to practically significant result. The food for reflections and doubts in occasion of capacity of criterion of practice is given also with ambiguous dialectics of social ideals and real our achievements what really we can just put the question: Are we aware that the relation of theory to the practice is dialectic?

Nevertheless, only the criterion of practice is absolute and defined and in the sense that it establishes objectivity of true, its results of true estimations appear finally in known frameworks and conditions. It is hardly logical to include in a definition the absoluteness of the criterion of practice and its uniqueness as the criterion of true. It is only consequence of absoluteness of

[1] Kasavin I.T. Descriptive understanding of true // Philosophical science, 1999, №8, с.66

criterion. All other kinds of the cognitive activity accepted quite often as a criteria of true, appear to be methodological principles according to its content, and according to the function and result of the content of objective knowledge is the criteria of error.

Introduction of the last concept in gnosiology is to expedient us. It is thought close to negative criterion of true of Kant as necessary, but not sufficient to the condition of objectivity of knowledge. Formal-logic, methodological principles are capable to testify of errors, sophisms, paralogism but do not guarantee the validity of representants and in this sense if true act as criteria, so they are not true but errors. If criteria of error (they are a lot) cancel inadequacy from knowledge, the criterion of practice besides accumulates in it true.

Opening the criterial functions of practice in the Marxist theory of knowledge, as a rule, reduce to one of them, that is the function of ascertaining of the validity or false of an image. It is thought, very important creative aspect - in fact criterion of practice thus is ignored, being a kernel of a substantiation of knowledge, provides its development, translating one cognitive form into another, transforming true in knowledge. This moment initiates the «last» «segment» where by means of criterion of practice the original knowledge of true, its substantiation and the simultaneous comprehension by the subject necessary for relative end of all dialectic way of «knowledge of true» is directly carried out. The last word-combination is not a tribute of Hegel manner of expression; German philosopher considers it as substantial, independent and necessary component of spiritual manufacture.

Thus, it is possible to speak about bi-functionality of criterion of practice in which there are two parties: criterial and constructive (creative). Often they are shown in indiscernible unity; more precisely are not shown but contained in essence. But when representation is false, function of criterion of true degenerates, degenerates in verification, ascertaining of its gnosiological definiteness. If the representation put on trial is true the practical criterion carries out subjective comprehension of its validity, reception of knowledge. The accumulation of knowledge is based on this creative function of practice.

One of the moments of Popper's falsificationizm is the denying constructive profile of function of criterion of practice. Reducing the content of science to the trues denied during their verification, Popper simplifies a gnosiological role of practice and experiment, seeing in them only verifying function. In essence Popper denies the true in itself, especially - achievement of knowledge by its transformation by criterion of true. All this deprives science of cognitive content and to a certain extent consequence of an identification of absolute and objective true[2] and non-recognition of dialectically capacious nature of criterion of practice. Really, from the presence of the objective content in true follows its absoluteness (actually, it is the same ideal content, objective concerning to the subject and absolute concerning to object), but the true includes cognitively uncertain and in this sense is characterized as well by relativity. Popper ignores similar interpretation of concept.

For the sake of justice we have to notice: Popper's concept appears as the panoramic picture of scientific knowledge manufactured by large stroke of paint-brush; he does not take interest in nuances. Concretizing its details further, it is possible to notice that to known methodological and world outlook preconditions of the given conclusions, one more is added. Even considering that circumstance that Popper carries out not gnosiological but epistemological approach to knowledge, and of a science the true has essential orientation, is focused on knowledge and expression of essence, its requirements to the given concept are represented strong enough, identifying the objective contest of true with true itself.[3] The rigid criticism of relativism and subjectivity of neo-positivists carries away Popper in other extremity (and that intention as was necessary to expect, eventually, has pull together it with a position of criticized).

To add, Popper carries out the maximal approach to the question of verification of the

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[2] See: Popper K. The true, rationality and the growth of scientific knowledge// Popper K. Logic and the growth of scientific knowledge. M., 1983.
[3] Popper is not alone here. Let's remember Heidegger: «The question of essence of true comes from the question of true of essence». Heidegger M. About essence of true.// Philosophical science, №4, 1989., - 103 p.

validity of knowledge. Without consideration limitations and uncertainty of practice as criterion of true, the founder of critical rationalism stays apart not only from necessary, though also subjective (as it considers) criteria of coherence, pragmatism (instrumentalism), conventionalism, etc., but declares insufficient for true knowledge both empirical and practical criteria[4] . That is why falsificationism as the method with all its efficiency and value in a science, does not specify true, but (i.e. it appears criterion of error) only testifies to unsuitability of the theory and necessity of its change.

The tradition in which practice is exposed to the analysis as a way of substantiation of knowledge, in the western methodology of a science is supported not only by pragmatism. For empirical knowledge it contains, in particular so-called fundamentalist and not fundamentalist theories of the justification. The first validity as criterion of cognitive forms select certain indisputable bases (on manners of criterion of evidence of Descartes). In some not fundamentalist theories results of a science correlate to practice. However, its essence and gnosiological functions are underestimated: criterial function is narrowed to revealing pragmatical utility at knowledge.

Stated above bi-functional criterion of practice is fruitful in judgment of a parity of true and knowledge and denies the known points of view: « knowledge and true are synonyms», or «knowledge» and «true» are not identical categories. Any true knowledge, but not any knowledge is true», or «knowledge is such result of cognitive activity which can be estimated as true or false». The conclusion is more logical: any knowledge is true, but not any true is knowledge.

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[4] Popper K. The true, rationality and the growth of scientific knowledge// Popper K. Logic and the growth of scientific knowledge. M., 1983., - 339-340 p.

LANGUAGE TRAINING OF TECHNICAL UNIVERSITY STUDENTS AS AN IMPORTANT COMPONENT IN THE INTERNATIONAL INTEGRATION PROCESS OF NATIONAL EDUCATION STANDARS
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Signing the Bologna Agreement in 1999, Russia entered a new phase in the reformation of the education system. Due to globalization the following objective was developed: to create an integrated extent European education system. «An incorporated association in the education system is an essential part of the cooperation community, united in different regional organizations to achieve the goals in economic integration, social unity and political security» (HSE, 2005).

According to the national policy in the higher education system, it is critical for an engineer to be capable of adapting to variable living conditions, analyzing situations, evaluating and finding solutions to initial problems, possessing communication skills and developing intercultural relations (Sorokovikh, 2004). The major question is to promote modern conceptual approaches in determining the strategies and tactics of Russian education system incorporation in the extent international education system. It has become clear in recent years that education is the fundamental basis in the individuality development of the future engineer who has to enter the global marketplace successfully and competitively. Therefore, as higher education plays the most significant role in the formation development of the future modern engineer, not only is education, as a whole, essential, but also his/her high competitive professional level as well. One must not exclude that fact that native language (in our case, Russian) and foreign language (English) is a vital factor in this process. Thus, international integration of higher education is interrelated with English language teaching.

Current Russian university education standards and requirements in English language teaching do not fully meet the international requirements in engineering education. The recognition of new English language teaching

approaches and reorganization in today's technical universities is vital.

However, it would be erroneous to blindly adopt foreign experience in English language teaching and mechanically introduce it into the Russian education system. Therefore, one of the main factors in constructing an integrated extent education system is to retain and develop the traditions of Russian higher education.

The modern English language teaching concept is also determined by individual orientation in language study. «The main aim in language teaching is to develop a person's distinctive language orientation, being effective in implementing intercultural communication» (Korjakovzheva 2002: pg 3-4).

APPLIED ASPECTS OF REALIZATION OF EDUCATIONAL STANDARD ON SPECIALITY «PSYCHOLOGY» CONSIDERING PRACTICALLY ORIENTED TECHNOLOGIES

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The system of higher education in modern conditions becomes one of the most important institutes of personal socialization, where education and development of professional turns to be a solid process, directed on forming of cultured, educated, able to create, to compete and socially active specialists.

Higher school is the main reproductional mechanism for spiritual and cultural national potential and personal development. It is base for bringing cultural and scientific achievements to next generation, it is condition of national security and progress in society development.

But as we see on practice, today's graduates don't have enough such important skills and personal features as independent critical thinking, flexible adaptation in changeable life situations, citizen maturity.

The reform of educational system has to be directed on deletion of existed demerits and contradictions because successes and failures in educational field used to reflect on whole society.

Final goal of education is declared in contemporary State Educational Standards of Higher Professional Education. It sounds as forming of citizen, professional and personal maturity of specialist. Therefore modern society has special demands to personality, one of the most important among which is personal maturity.

The system of higher education of psychologists is being criticized for distortion in direction of so called «academic» paradigm. Traditional contents of psychological education include rather fundamental psychological preparation which combines with minimal practical part. Even when we analyse such formal marker as quantity of educational time, determined by State Educational Standards of Higher Professional Education, we see, for example, that students with educational program on speciality «Pedagogics and Psychology» (050706) have number of weeks given for practical works equal to 20 and for theoretical course the number of weeks is equal to 156 (that is almost in 8 times more). Students with speciality «Psychology» (030301) have 180 weeks assigned for theoretical course and 25 weeks assigned for practical work (that is more than in 7 times less). Therefore such disproportion between «theory» and «practice» (with vivid prevalence of theory) is basically already laid in educational standards.

Also this situation is not characterized only by lack of time assigned for practical courses. The educational practice contents are also being criticized. So, M. M. Balashov, M. I. Lukyanov emphasize its fragmental nature, its limitation by one or two fields of professional activity. We also want to mention lack of student's initiative in the matter of choice of topic and base for their practical courses.

Actuality of named problem is activating the search for new educational models which could combine in harmony academic and practical paradigms of psychological education (G. S. Abramova, I. D. Badmaev, I. V. Dubrovina, V. Y. Lyaudis, R. V. Ovcharova, A. V. Petrovskiy, V. I. Slobodchikov and others). As we suppose, the solution of this aim could be

realized by addition to academic education a specialized preparation on material and in conditions of certain professional environment, organized in form of extra lecture-hall lessons.

In foreign researches the named problem has been solving by involving students of the humanities in socially useful activity (M. G. Gray, A. K. Optadge, R. Friker, S. Heshvindt, Sh. P. Klein). Unification of socially important service and formal academic learning is being realized in so called «Service Learning» programs.

Since early 1960-s the Service Learning programs have become actively incorporated in post diploma educational practice in USA and other countries. In such countries as Argentina, Portugal, USA programs of involving student youth in socially useful activity have been accomplished on the state level.

The principal directions of Service Learning programs are:

1. Assistance in increase of educational quality in Higher School Educational Institutes: rising of motivation to learning, increase of effectiveness of educational-developing process, preparing of specialists needed on contemporary labour market.

2. Personal development of students and their professional establishment: rising of self-esteem, self realization, getting possibilities to apply given knowledges in practical work with further receiving of working place.

3. Forming of student's citizen position, creation of clear example of young people's active positive involvement in life of their country.

4. Social support: involvement of students in organizing and realization socially useful activity in their own city, effective use of academic knowledges for pro-social activity.

In Russia elements of this program have found their application only during last decades of XX-XXI centuries. Development of Service Learning programs supposes accounting the specifics of Russian higher educational system, developmental level of incommercial municipal organizations, relation of young people to social activity. In general, elements of Service Learning program have started to be used by rapidly developing social organizations.

As we think, this scheme is rather spread in Russian higher educational institutes but by other names. For example, V.G. Chaika offers specially organized extra lecture-hall work program for students. In his researches students as volunteers were taking part in psychodiagnostical procedures, psychological consulting and training with pupils of 5th-11th classes of schools providing general education.

The results of experiment show that specially organized independent work of students leads to increase of educational effectiveness and positive changes in their motivational structure.

In system of professional preparation for psychologists one of the first places take practically oriented technologies of organization of practical work system which provide unification of theoretical preparation of future psychologists with their practical activity in social institutes and organizations, institutes of education, culture, health protection, business and state government.

Practical work is various by its contents and is based on principles of persistence and differentiation. Each kind of practical work has its particular aim: to prepare a specialist who, besides needed supply of knowledges, skills and experience also has ability to use them in his work effectively.

Practice promotes to increase a professional mastery of students, to develop skills of managing, organizational, diagnostic, correction and upbringing work. It helps future psychologist to realize his personal features, to take an initiative, to display creativity.

Professional training of specialists is inconceivable without getting by them common professional practical skills. Developing of common professional skills is taking place during the period of studying practice, which represents an accomplishment of complex studying goals included in separate program.

Industrial practical work supposes for student an independent accomplishment of certain educational and industrial goals (tasks) in condition of enterprise.

Final stage in higher educational preparation of psychologists is the diploma projecting – an accomplishment of complex task, which result is being presented to State Examination Commission in form of diploma project or diploma work.

A part of diploma projecting is pre-diploma practical work – an amount of time

during which student has to complete the industrial part of given task (gathering of material, conducting of experiment, etc.).

This division in kinds of practical preparation is quite conditional and is done with the purpose of making clear methodic functions usual to separate kinds.

Student's practical activity allows to solve educational and real practical goals during the same time. That is why an amount of tome given for one or another kind of practical work has to be considered as a period when that kind of practice is predominant but is not the only.

Basic directions of activity in improvement of practical preparation system for psychologists should be considered as:

- Rational spreading of kinds of practical preparation during educational period, relating to their volume;

- Creating a system of methodical support which could orient teachers on developing specific work plans of one or another kind of practical preparation and also which include educational and real practical goals (tasks) developed by teacher;

- Intensification of connection between practical preparation and future industrial activity of young specialists and also intensification of connection between theoretical educational course and practical activity of student who is learning within the industrial process;

- Deepening of practical preparation in development of organizational skills, getting an experience of working with people.

Successful activity in these directions is based on intensification of methodical work, strengthening of connection between education and industry, activation of teacher's role in practical preparation of students. Therefore we can see that kind of strategy of educational process organization which, as A. M. Matiushkin said, leads to such results when development of cognitive activity is being accomplished not in form of learning different ways of solving problems but in form of development of creative thinking in conditions of didactically organized dialogue and group thinking. The first object of changing is the level of self-regulation of whole educational activity – self-organization of educational aims is being realized, motives of learning also change their whole structure.

It's important to notice that all these new formations of individual and collective mind have not only narrow situational character but are spreading far over the borders of concrete educational situation. It's not accidentally that in practice of modern institutes of higher education productive creative forms of organization of collective educational process are so well spread. Industrial teams, student construction bureaus, building brigades, student scientific research laboratories and so forth make character of education and character of work activity more and more close to each other in aspects of their social structure and direction on achievement product of full cultural value.

FORMATION OF STUDENTS' COGNITIVE SELF-DEPENDENCE IN "HIGHER EDUCATIONAL INSTITUTION – ENTERPRISE" INTEGRATED SYSTEM AS A PEDAGOGICAL ISSUE OF CURRENT IMPORTANCE

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Integrated systems of education employed in Russian higher education system are associations of educational institutions of higher education or their branches, departments, faculties, sub faculties and manufacturing firms or organizations which implement specific educational programs of higher education and conduct internal and internal-correspondence (evening) training in combination with students' labor activity aimed at formation of professional skills in specific specialties and training programs. Integrated systems of education ensure raising the level of the students' professional skills and theoretical knowledge in real working environment, promote mastering and application of creative approach in fulfilling their professional duties, which means they

accomplish important tasks of raising the quality of engineering education.

Student's cognitive self-dependence is an attribute of his or her intellectual faculties for learning ensuring in the future an active desire to acquire knowledge and apply it in action.

Analyzing the present research in the field, one can conclude that many aspects of forming students' cognitive self-dependence in higher education haven't been properly developed yet. In particular, distinctive features of forming students' cognitive self-dependence in the integrated system "higher educational institution – enterprise" haven't been displayed.

While keeping a certain amount of knowledge and skills to be acquired by the students, curricula of technological higher educational institutions do not focus enough attention to students' independent work. Such facts as the number of students capable of acquiring a given amount of knowledge at the expense of previous training, how much time is required to learn presented teaching material are not taken proper account of. It is also essential to consider that in the present economic conditions the opportunities of learning at Universities of big cities have become lower, and establishing branches of higher educational institutions in small towns, which is, on the one hand, a positive factor because the principle of accessibility of higher education for all is applied, on the other hand, brings to increasing the number of students from rural areas, whose level of cognitive self-dependence is rather low.

In training future specialists at technological higher educational institutions the issue of the day is the lack of the students' ability to use the potential of basic knowledge base for problem solving. Acquiring a certain amount of scientific data on the reproductive level still remains the aim of studying a field. In the meantime the purport of learning a discipline is to make a student in the first place grasp the material and in the second place make him or her familiar with the process of acquiring the learning material and methods of operating the received knowledge.

The problem of transition from acquiring a ready knowledge to acquiring knowledge useful for the students' future professional activity based on the students' cognitive self-dependence remains important.

The theory of developing teaching justly referred to by A.P.Aristova, P.I.Pidkasisty, N.A.Polovnikova as reproductive and creative theory of training cognitive self-dependence, is the theoretical basis of forming students' cognitive self-dependence. According to this theory, orientation of the teaching process toward potential abilities of the students and realization make them master new skills, acquire new knowledge, create new schemes of problem solving, new ways of activity. The main tasks of an educational specialist in this process is to organize educational activity aimed at formation of cognitive self-dependence, formation and development of students' faculties, their world outlook. It is important to establish connection between professional activities of an educational specialist and cognitive activities of a student aimed at attaining the set goals. Acquiring knowledge, formation of faculties and skills, development of creative capacities of students are interrelated processes, but their unity and development are achieved by means of purposeful efforts of an educational specialist. Consequently, cognitive activities can be both productive and creative. Formation of this faculty of students can take place both during conveying knowledge and students' independents research.

Students' self-dependence shows itself in different ways. There is still no unanimous understanding of the essence of students' cognitive self-dependence. For example, in researches by G.N.Kulagina, students' self-dependence is of intellectual nature, it determines only procedural form of their activity and doesn't reflect volitional and motivational factors. "Students' cognitive self-dependence is, first of all, independent thinking, displaying itself in the ability to understand a problem, a task, and in finding its solution, in the ability to make conclusions out of received knowledge, to pick out what is the most essential and crucial" [1].

Speaking about the formation of students' cognitive self-dependence within the system of "higher educational institution – enterprise" it is necessary to consider different approaches to way of practical solution of the problem. It is important to form students' cognitive self-dependence on the basis of the theories by B.G.Ananyev's, Yu.M.Kulutkin, E.I.Stepanova, G.S.Sukhobskaya and others, according to which people combining studies with industrial activity

(as in case of the integrated system "higher educational institution – enterprise") extend their attitude to practical activity to their studies. It displays itself in the fact that students begin to consider the process of studying as a self-educational one, the one they involve themselves in with moral certainty. They become discerning and capable of self-control and self-regulation in this kind of activity. Knowledge is considered by them as a means necessary to solve different kinds of problems arising in their lives.

ORGANIZATION AND CONTROL OF STUDENTS' INDEPENDENT WORK

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One of the most important issues of the educational process is independent students' work. In the sphere of high school pedagogy the following law says: students' knowledge is the result of their own cognitive activity. That is why the main task for high school activity is to teach students to get knowledge.

The effective independent students' work depends on the way of its organization, necessary methodical material, and tutors' control which is important for first-year and second-year students because of the low knowledge level in science subjects and inability to work on their own. Our activity of teaching freshmen to work independently is the determining factor in their personality formation, their future ability understand scientific and technical texts, to solve scientific and engineering problems of different levels.

The tutors of mechanics and engineering department use different methods in organization independent students' work, for example: fulfillment of individual and calculation tasks, tests given in the beginning, throughout and in the end of the academic year, computer tests, paper works, writing summaries on the basis of theoretical material, making researches and so on. The fund of testing materials is created for working though practical skills.

The question of students' independent work (SIW) control is also relevant. The SIW control should be regular, objective from the point of view of quality and "quantity" of the learnt material. Some types of control can considered to be rather effective.

The SIW will be effective in case if it is intended to get a particular aim and to be self-controlled. The method of students' knowledge self-control is used by us. For this purpose we use testing programme "Symbol" which was worked out in Tomsk Radio Electronics University. The "Symbol" allows to put into practice efficient knowledge control and self-control, gives the opportunity to get quality and quantity of learning. It is important to point out that this method can be used even among students not making satisfactory progress. The self-education process catches the attention of "indifferent" students. It is possible to use individual and group knowledge level tests of the current course because of the "simple" organization system. The use of instant self-control system allows to solve many problems in educational process: for example, overcoming of psychological barium in learning, rise of self-esteem, development of students' independence, that means: a student develops his skills himself, studies the necessary material, controls, values , checks and corrects his cognitive activity. This method corresponds to the modern concept of education.

THE IMPORTANCE OF FUNDAMENTAL APPROACH TO STUDYING PHYSICS AT UNIVERSITY

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Natural science is based on physics laws because physics is a science which studies the simplest and more general rules of natural phenomena; properties and construction of matter and laws of its motion.

Physics as a science of natural phenomena is the basis of the whole contemporary natural science. It takes the extraordinary place in the general knowledge system accumulated by the mankind. Physics demonstrates that very ideal to which any sphere of knowledge must aim for when being founded on a comparatively small number of experimentally proved principles and powerful mathematical system one can logically and strictly deduce a lot of consequences and precisely predict the final result of the process by initial data.

Study of physics plays the important part in formation of a present-day engineer of any technical field because cognition of physical laws fosters the development of sciential outlook and lays the foundation for learning special disciplines [1].

At every moment, physics as any other science, can be characterized by the following general layout: 1) methods applied in physical research and resulted findings; 2) the main concepts generated by physics by the given moment as well as theories developed on their basis; 3) the main research problems and trends; 4) physics branches leading to other scientific branches and practice. Each of these elements contain, as a rule, both general features peculiar to any science branch and specific ones peculiar to physics alone. Principles of definition of physical theory have two features: 1) clear and precise requirements the theory must satisfy; 2) substantiation by metascientific arguments. The example of these principles is the requirement for physical laws which must be expressed by a mathematically precise quantitative form for physical theories to have consequences available to experimental testing, etc. [3].

A method when the main elements of teaching correspond to those ones of scientific knowledge is the most rational method of teaching physics. The present-day process of learning physics must include both classic conventional methodologies (lecture material; laboratory course; tutorials; seminars, etc.) and up-to-date computer technologies.

Here belong numerous testing works. However, these attempts have not given serious results. During the past years, testing methodology has been decreased abroad. Prof. A. Wolf [2] considers that today testing result conclusion must not be categorical or too strict. According to Prof. K. Tailor (USA), "…As a result of testing, one must be aware of missing a talent or attracting to teaching those who will feel discomfort or uneasiness entering educational programme for gifted students".

It goes without saying that a qualified use of computers is the times dictate. However, computer is only an instrument for derivative tasks solution. It is, nevertheless, a means to achieve the definite purpose, and there is no need to make of it an end in itself, especially in an educational institution. A vast computerization must be combined with wariness in choosing software and definition of the optimal amount of classes with the use of computers. Computer technology in education gives much opportunity to improve teachers' and students' creativity.

Computer technology application allows modifying the entire educational process and implementing the model of a person-oriented teaching. Up-to-date educational technology (computers, telecommunication, software, methodology), strengthening of different educational forms are of the greatest importance for students' self-training in the capacity of methodological and organizational provision. Courseware must be generally accepted, distinct and efficient.

General application is achieved by a detailed statement of the subject; fragmentation of the material into portions of information interconnected and comprehensive to students; detailed explanation of the content.

Distinctness of the courseware is provided by its algorithmic structure following from the logically stipulated way of presentation of the teaching material.

Task solution on physics is a necessary basis for studying physics because it is connected with the independent work which, in its turn, teaches to analyze the phenomenon under study. As a result, a solving of any simple task promotes the development of sciential outlook and approaches to the model of scientific physical exploration.

Task solution on physics requires knowledge of physical laws, methodological approach and analysis. Except general methods of solving, each part of physics contains specific approaches to it connected with peculiar features of physical phenomena presented in the given part. In the process of task solution theoretical problems are always touched and task solution of any level of complexity leads to theoretical generalization.

This approach to solving problems is presented in such classic methodological aids as "Physics exercises methodology at a higher educational institution" by E.M. Novodvorsky and E.M. Dmitriev; "Task solution manual on General Physics course" by E.V. Firgang and some others. In fact, accomplishing a task we study physics and see its beauty.

Knowledge of physical laws implies skills not only to formulate them but also apply them in specific cases when accomplishing tasks. However, it is solution of tasks that presents more difficulties for those who study physics. Formal knowledge of laws is not, as a rule, sufficient for solution of tasks. In some cases, knowledge of special methods is required to solve specific groups of tasks. The main thing that facilitates a success (except knowledge of theory) is the ability of analytic thinking, i.e. skill to discuss. These facets are not always given due attention at tutorials.

Education offered by a university today is characterized by a lot of information which can not be learned during a comparatively short period of education if it was not regulated on the fundamentally new basis. Generalized methods, methodological principles, ideas, etc. applied systematically and on the large-scale to the educational process, can serve as this basis. In solution of physical tasks, this approach was implemented by Prof. B. Byelikov that is founded on the system of the most general ideas of physics as applied to a solution of any physical task.

It is Prof. B. Byelikov's opinion that in order to successfully accomplish physical tasks it is necessary to acquire generalized knowledge in addition to specific ones. The basis of generalized knowledge is fundamental ideas of physics having methodological nature. Fundamental ideas in physics are rather not numerous, namely: physical system, physical quantity, physical law, state of physical system, interaction, physical phenomenon, ideal objects and processes, physical model, etc. A connection of physical phenomenon with all other fundamental ideas is of great importance. The use of the fundamental ideas system allows formulating the most important definition of a theoretical physical task as a physical phenomenon in which any connections or quantities are not known. To accomplish a physical task means to restore unknown bonds and detect required physical quantities. This detection is of great methodological meaning. In case a physical task reflects some physical phenomenon or a group of them, it is desirable to have not only an idea (specific knowledge) of it but also be able to analyze any physical phenomenon. The process of the task solution can be divided into three stages: physical (it is completed if a closed system of equations is equated); mathematical (obtaining of solution in general and numerical form); analysis of solution.

The physical stage begins from familiarization with the task situation and physical analysis of it that is concluded in determination and analysis of a physical phenomenon. The introductory part of the analysis is of auxiliary character; it is like entering the world of physical phenomena described in the task. The analysis of phenomena is carried out at the stage of preliminary familiarization with the task. In this case it is necessary to make a draft with all given data and sought quantities. A draft helps to graphically present the given physical phenomenon. Already in the main part of the physical stage it is necessary to analyze physical phenomena. As it is known, a physical phenomenon contains qualitative and quantitative aspects. That is why the qualitative nature of the phenomenon must be defined in the first hand (essence, process, etc.). Here, firstly, a learner must choose a physical system; secondly, define qualitative characteristics of these objects; thirdly, consider

what physical processes these objects are involved in. Then, quantitative bonds and correlations between different physical quantities should be stated which describe the given phenomenon. Quantitative bonds of different physical quantities are reflected in physical laws. Therefore, the use of the proper physical laws allows obtaining the closed system of equations. After it was carried out, the problem is considered to be physically solved.

The mathematical stage begins with a solution of closed system of equations and ends by obtaining of a numerical answer. This stage can be divided into two ones, namely: a) obtaining the task solution in general; b) obtaining the numerical answer of the task. Having solved the system of equations a student can solve the task in general. After arithmetic calculations he/she obtains a numerical answer. A physical element is almost absent in the mathematical stage. Undoubtedly, the mathematical stage is less important than the physical stage, however, it should be noted that it is not secondary one. After it, the analysis of solution stage follows. This stage is often impossible to be carried out if the numerical answer was not obtained. Thus, for the achievement of the final physical task solution, the physical and mathematical stages are required equally.

After obtaining a general solution and numerical answer the stage of solution analysis is carried out. This stage is characterized by clarifying of how and from what physical quantities depends the sought quantity; which conditions this dependence satisfies, etc. After the analysis of the general solution, a possibility of carrying out other tasks is considered by means of changing the given task situations. The analysis of solution is some creative process; therefore, its method must not be very strict and can include a range of other elements depending on the task situation. The analysis of solution is closely connected with the method of the task statement.

The system of stages of task solution is not a separate entity. It is directly connected with the problem of the method system for task solution on physics. The case is that at each stage a student must carry out the appropriate independent work. For students to learn the task solution process on physics, it is necessary to do this on their own. If a student was not informed about the general methods of the task solution, he/she will use the cut and try method. Therefore, it is necessary to carry out all stages of the task solution as a way of the independent activity of the learner. Thus, the system of general methods must be characterized by the following: a) universality, i.e. to be applied to any task from the general course on physics; b) coverage of all stages of the task solution.

Within the rapid development of the scientific and engineering revolution, the part which plays physics significantly grows not only as an engineering science producing industrial branches but also as a basic and world outlook one. A need for physical knowledge for specialists qualified in natural and engineering sciences is obvious [5]. Among general education subjects, the course on physics offered by a university takes the important place in training specialists since their competence is defined not only by the scope of acquired knowledge but also the level of comprehensiveness of general laws of science and technology development; scientific thinking skills; ideology. Learning general physics gives the opportunity to future specialists to form their ideology and develop scientific thinking.

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REFLECTIVE APPROACH TO ADAPTIVE ACADEMIC ENVIRONMENT AT HIGHER SCHOOL

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Nowadays one of the most important problems of the Educational System is that of finding ways of teaching quality improvement. This problem, first of all, concerns Pedagogical Higher Schools. It is the graduates of Pedagogical Higher Schools who should solve the problem at the level of upbringing and developing our younger generation.

Thus, the Pedagogical Higher Schools face the question of qualified professional future subject teachers' training that is in accord with the demands of the person, society and state.

In this connection it is necessary to reorganize the teaching process at the Higher School with the purpose of creation conditions for professional competence formation at students.

Realizing the fact that every student is an individual and inimitable as a personality, there appears a need to create an adaptive educational environment, in which the student himself defines the trajectory of his development considering his individual possibilities and capabilities; the idea of self-education being taken as the basis. Let us mark that the adaptive educational environment involves all the components of the educational content: knowledge, activity experience in familiar situations, creative activity experience and the experience of emotional and ethical relations to the world. It underlines the importance of principally new approach to the teaching, which is oriented not only on digestion of special knowledge and skills by the students, but also on the development of the person and its capabilities, and the enrichment of its individual experience. By the way, it is important to remember, that the adaptivity of the educational environment includes the result system adaptivity as well, and it necessitates the meaning change of the educational process itself.

Thus, it is urgent to plan the conceptual and processual components of the adaptive educational environment on the basis of a reflective approach to the process of teaching.

It is connected with the fact that the very reflective activity will let the student realize his individuality, originality, unicity, and destination, and form his professional competences in the conative, cognitive, active and personal levels. Such an approach corresponds to the meaning of the notion "education" as the formation of the "ego" image.

In this connection the following components should be included into the process of teaching students:

1. A technological map, representing a passport of the future learning process for a student, where its principal parameters providing the academic success are shown integrally and concisely.

2. The technology of the reflective approach, on the basis of which the achievement of strategic aims is realized.

3. Means, methods and techniques, which will be used while reaching the strategic aims.

4. The management system, representing a cooperatively distributed activity of the teacher and the student.

However, it should be noted that every technological stage of the reflective approach corresponds to a definite strategy sort represented as some certain toolkit (step-by-step algorithm) aimed at students' professional competences formation.

The organization stages of the educative process in the frames of the reflective approach can be represented as follows:

Stage I. The definition of objectives in the process of cooperatively distributed activity of the teacher and the student.

Stage II. Research, understanding and re-evaluation of the information by the students and organization of communicative activity on the specification of the problem by the teacher.

Stage III. The information interpretation and projecting a new method of action.

Stage IV. Including the new method of action into knowledge system.

Stage V. Self-evaluation of the activity by the students.

Stage VI. The substantiation of the defined objective achievement.

It is out of doubt that such an organization of the educational process will help the student to see his destination/mission in the academic process more vividly, to form his professional

competences and to follow his individual development.

Generalizing the above said, the conclusion should be done that a reflective approach to the process of education, because of its flexibility and effectiveness, allows using the reserves of the educational process itself and the students participating in it more rationally

PROSPECTS FOR NEW E-LEARNING EDUCATIONAL TECHNOLOGIES IN A TECHNICAL INSTITUTION

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Recently the demand for training using new e-learning educational technologies has grown considerably in the market of educational services. E-learning (electronic training) is one of the major advances in the educational system, combining active Internet inclusion into online and offline training process, set of informational and telecommunication technologies, software package and electronic version of textbooks [1-3].

A part of the existing potential of electronic training is represented by the following: methods of multimedia integrated on-line and off-line process of getting knowledge, training based on web technologies, providing electronic versions of research and teaching information, necessary for the training process, audio and video support for the material taught, establishing of intercontinental exchange of experience in the field of the latest achievements in modern high-technology educational process by means of distant video and electronic seminars, conferences, workshops, forums, as well as electronic publications.

Analyzing the students training process in a technical institution with the use of innovative e-learning technologies we can mention the following most positive and important factors:

relevance of the technologies used to modern means of intellectual activity, their availability, industrialization, unification and standartization, integration of national educational systems. Electronic educational technologies are becoming one of the promising trends, able to meet the need of modern information society for high-quality knowledge as a product.

Thus, e-technologies provide integration between distant and traditional arrangement of the training process and allows to shift emphasis in the relations between a teacher and a student. It also helps to implement a systematic approach to provide students with all necrssary teaching aids. Extra opportunities appear to improve the quality of teaching students living in remote locations and to attract staff in different regions to the process of education. E-learning gives choice in terms of the type of the course and the speed of learning. Universities are able to adapt the content of the courses offered to economic and social conditions and provide continuous education after graduation from the university [2, 4].

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PROFESSIONAL PSYCHOLOGICAL ADAPTATION OF TEACHERS IN EXTREME CONDITIONS OF THE NORTH OF RUSSIA.

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Efficiency of work of the person is substantially defined by his adaptation to conditions of activity, factors of medium. For this reason the major pragmatical purposes of studying of mechanisms of adaptation are a prediction of a course of adaptation in a concrete situation and exercise of external correction of this process for its optimization.

Studying of a level of intensity of pedagogical activity has shown, that work of the teacher demands high qualification that is connected with necessity constantly to seize new knowledge, with a high degree of the responsibility for results of work. Teachers constantly meet set of disputed situations within the working day. Work of the teacher is closely connected to necessity of the constant interpersonal interaction influencing efficiency of activity.

In a situation developed for today in educational system, problems of adaptation of the teacher, criteria of an estimation of his person are allocated with insufficient attention of psychologists. Researchers in the greater degree dealt with problems of success of pedagogical work, skill, professionalism. If to take into account difficulties of climatic conditions in which teachers of regions of the Far North the theme of pedagogical adaptation becomes especially actual live. It speaks that in conditions of the North this theme was not studied earlier, and the requirement for the given researches stands is very acute.

Course of biological processes at the person it is caused by a lot of factors: character of labour activity, a degree of formation of the cogitative and speech systems determining social essence of the individual. Such aspect of research enables to penetrate into existence of adaptive mechanisms which provide to the person an equilibration of his organism with an environment. It is active process of the adaptation of an organism on overcoming injuring action of an environment.

In what good cultural and community conditions there was a person, the climate is that natural background which accompanies him not only in conditions of severe weather, but also in conditions of a house and manufacture. In adverse conditions of an environment in an organism there can be the various adaptive shifts occupying at times an intermediate position between norm and illness. Fluctuations of barometric pressure, change of humidity, the factor of illuminating intensity, - all this, undoubtedly, causes compensatory activity of many systems of the organism, connected with those reactions which are caused by public - labour activity.

Climatic features of the North inevitably cause functional fluctuations in an organism of the majority of people living in an extreme environment. There is no doubt, that reactions of an organism to influence of a cold basically are directed on the adaptation to an environment. Striking contrast of seasons, periodic repeatability of long colds in a year cycle of the nature challenge the person, will mobilize his physical and mental forces on adaptation to a rigid rhythm of life. The person of the North is as much as possible entered in this cycle. It defines phases of work and rest of the person, his strain and a relaxation. Life in extreme conditions becomes arrhythmic and fragmentary intensive. The long winter and long night alternate in the short summer and in the long afternoon. Thus, work of the Norilsk teacher is complicated with factors of medium which probably and are a handicap for successful adaptation to a professional vital way.

In conditions of Far North at teachers specific features of psychological adaptation which affect the attitude to a professional vital way, health, to as to the person, connected with increased requirements to adaptable opportunities of the person are marked.

In our research psychological adaptation is surveyed as the process reflecting the attitude to a professional vital way, to professional work, and determining a measure of success of interaction of the person with changes of conditions of medium. Professional adaptation is shown in change of an internal position concerning itself in activity and all vital way, and also change of the

activity in creation of life. Thus, professional adaptation is surveyed as an integral part of adaptation to life as a whole.

During professional adaptation of the person various lines of his ontogeny which harmonization is the main task of practical psychology are bound. For today it is known, that teachers are professional group which is especially subject disadaptive to tendencies. Many scientists (M.A.Berebin, L.I.Vasserman, G.F.Zaharov, L.M.Mitin, A.A.Rean, L.N.Sobchik, etc.) Mark, that professional work of teachers is one of the most intense (in the psychological plan) kinds of social activity. Work of teachers is included into group of trades with the big presence of stresses - factors. It agrees to the data of modern researches each tenth teacher has stepped over a side of mental norm, two from three are subject a various sort to nervous breakdowns. The disadaptation covers not only sphere of health: 90 % of teachers are focused on the last life, at them is reduced креативность (Korzhov by E.JU.psycholog of adaptation of teachers to professional work. СПб.: the Baltic pedagogical academy. Institute of psychology of the person. 1996, With. 3). Especially typically for teachers infringement of the personal integrity shown first of all in behaviour of the teacher as extremely carrier of social qualities.

At research of physiological functions at persons occupied by intense brainwork with high nervously - an emotional load, by the end of work (moreover and in extreme conditions) are marked sharp intensifying adrenergic the influences considerably raising the general level of activity of functional systems and, augmentation of cardiovascular reactions. Such dynamics of physiological functions represents intensive mobilization of power resources of an organism and is estimated by many researchers (P.K.Anokhin, G.L.Apanasenko, M.A.Grishchevsky, A.I.Kikolov, A.I.Kovaleva, V.V.pike perch, etc.) as adverse. Hypermobilization frequently results in an overstrain and an attrition regulatory mechanisms, to occurrence of prepathological and pathological conditions.

The concept of psychological adaptation as process which supports dynamic equation in the man-habitat system, allows to reach the greatest possible efficiency of behaviour of the person and his physiological maintenance, it is possible to survey as a basis of the systemic approach to research of professional work.

At the analysis of professional efficiency adaptation is estimated at a level of that microsocial medium in which the behaviour is immediately realized. In this case adaptable value of adequacy of microsocial interaction is precisely shown. At the same time, intensity of professional work is closely connected to all three aspects of psychological adaptation, demanding the realization and conservation of a psychological homeostasis, steady purposeful behaviour (actually psychological adaptation), adequate interaction with other participants of activity (social - psychological adaptation), an optimum ratio between psychological and physiological adaptable processes (psychophysiology).

The adaptable approach to professional work provides the account of many-sided nature of professional resources. Now in the literature necessity of revealing of adaptable features which result in those or other results of activity, correlations of personal and professional development in uniform process of a becoming of the person is even more often marked. The problem of an ontogeny today leaves on the foreground of a psychological science.

Psychologic-pedagogical adaptation is understood as process of active interaction of the person of the teacher and the professional medium, directed on maintenance of their dynamic equilibrium by a principle of a homeostasis. Psychologic-pedagogical adaptation is characterized by two groups of factors:

• Objective factors of professional adaptation is a professional - pedagogical medium. In attitude to psychologic-pedagogical adaptation is a pedagogical microenvironment (colleagues, a management, pupils, and also conditions of process of training). By professional medium besides a microenvironment it is possible to relate and internal medium of the teacher as persons and the professional. In that case psychologic-pedagogical adaptation consists in harmonization of the private world.

• Subjective factors of psychologic-pedagogical adaptation of the teacher are general and special readiness, features of character, type of temperament, a degree of form mental processes, functional conditions, displays of abilities, a psychologic-pedagogical orientation,

age, a state of health, a personal position and others.

The adaptive medium is defined as set of physical and social variables of an external world. It is frequently emphasized that adaptation is multilevel process and in this connection necessity of its complex studying. It is possible to allocate during adaptation levels high and low; levels of adaptation to макро and a microenvironment, to itself; physiological, personal, social; climatic, personal - psychological, social, a level of interpersonal dialogue, a level of adaptation to pedagogical system (to new demands); external (training to new samples and ways of behaviour) and internal (acceptance of new forms of behaviour and views), and actually adaptive and disadaptive. In the latter case it is possible to base on classification of conditions of adaptation of S.B.Semichova:

а) Adaptation;

б) A condition social mental   And somatic intensity – threat of a disadaptation;

в) A partial disadaptation (preillness and group of "risk");

г) A total disadaptation.

Psychologic-pedagogical adaptation in conditions of multilevel preparation assumes:

• high adaptable potential of teachers for exercise of an individual approach to pupils,

• skill to be guided in diverse collectives of pupils, with different readiness, with different personal, age, social features, with different group unity,

• skill to behave in difficult situations,

• readiness to teach on a high level it is especial at finishing stages of training.

Pedagogical activity in conditions of multilevel preparation of pupils assumes sharp augmentation of a stream of the information, reorganization of an operating mode, necessity of an adapting to new conditions of activity, reception of great volume of knowledge and a complex of skills. These are the factors causing an overstrain of the central nervous system, development of a stress. The information stress is shaped in a situation of information overloads, the emotional stress arises under influence of alarms, conflicts to pupils and colleagues. Not a secret, that the best agent of struggle against harmful consequences of a stress – work in which the person as much as possible realizes itself as

the expert. On L.V.Smolovoj's dissertational research, some social factors accompanying teacher's work as influence fastness to a psychological stress.

Psychologic-pedagogical adaptation has two stages: preparatory and immediate.

The preparatory stage is characterized by readiness of the teacher for activity. It proceeds during training. Immediately the stage of adaptation demands from the teacher of knowledge and the skills necessary for any principal. The course and results of adaptation depend, first of all, on a level of readiness for carried out tasks. Moreover, psychologic-pedagogical adaptation grows out psychologic-pedagogical readiness for activity which is surveyed as a special case of psychological readiness for effective activity and it is represented as professional - adaptable potential. Adaptation also is an objectivating of readiness, its display in concrete conditions.

Situations of professional work take an essential place in a vital way of the person. Traditionally and adaptations judge success, first of all, on включенности in professional work which renders appreciable influence on development of the adult person, being the important factor of efficiency of adaptable process. Professional work represents one of the brightest forms of interaction of the person with social medium. The trade of the teacher is widely wide-spread. Work of the teacher is characterized by the high responsibility and intensity. In comparison with other professional groups among teachers the risk of occurrence of neurotic frustration is highest, most the high level of "accumulation" of serious forms of neurosises here is marked. Teachers – group with risk of occurrence not only psychological, but also somatic frustration. Among them the set of symptoms of professional combustion, emotional instability, disharmony of person are wide-spread. Socially - disadaptive factors are low social security and prestige of a trade, necessity of professional interpersonal interaction in conflicting situations, information overloads, multifunctionality of social - responsible activity. In the literature a mention of social - psychological characteristics of teachers meet, as a rule, in connection with the description of their typological features, alongside with personal.

The professional disadaptation of teachers represents a serious social problem. All know, that value of work in human life is difficult for overestimating. The major are closely connected to work amounting health, well-being and life as a whole. Work should inspire the person, promoting disclosing of his personal potential. However, work can result and in occurrence of a condition of weariness at absence of the correct organization of work and the rest, the adequate attitude to and another, at the careless attitude to the organism. Last years scientists even more often address to the analysis of concept of the organizational stress connected to professional work, a load on work, distribution of duties, interaction with colleagues, roles, plaing on work. In this connection pertinently to consider also concept of adaptable norm of the health representing a functional condition of an organism. The functional overstrain can result in failure adaptive - compensatory the mechanisms directed on conservation of a homeostasis and development of certain adaptive behaviour.

It fixed, that the augmentation of the experience of work and age of teachers, ascending of a professional load (sometimes compelled on the social and economic reasons), inevitably result in accumulation of weariness, increase of alarming experiences, downstroke of mood, to vegetovascular frustration and behavioural failures. These clinical-and-psychological displays underlie frequently a psychological set of symptoms of "burning out" observable at teachers, as emotional and intellectual истощенности, the reduced serviceability to depressive experiences. Teachers are a group with risk of occurrence not only psychological, but also somatic frustration. High emotional loading the teacher frequently promotes occurrence of this set of symptoms which can be first attribute of a disadaptation.

Severe climatic conditions of Far North, ecologically unsuccessful situation, deterioration of a social situation result in essential changes not only physical, but also mental, social health of the teacher. In frame of morbidity of teachers in conditions of Far North mainly have a place cardiovascular and oncologic diseases which parameters are higher, than average on the country. The north and ecological features of region negatively influence and the genetical mechanism of the person, the number of children

with a pathology of members of digestion, vision, audition, endocrine, nervous systems grows. In connection with that, specificity of teaching activity grows and the differentiated approach in pedagogical system is staticized. Large number of functional distresses is a marker of unfavorable influence of a climatic, ecological and social - genetical situation. The tendency to breaking processes of social - psychologic acclimatization shows. Therefore there is a question on a problem of a disadaptation in educational space. It is natural as to believe, that in such climatic conditions rather often "breaks" of physiological timeserving mechanisms here again various meteorological distresses should be observed should meet especially frequently. However medical practice speaks other, that in extreme conditions of the North the organism of the person has colossal ability to adapt for aboriginal climatic conditions. Its physiological mechanisms of an equilibration with an external environment are capable, apparently, are reconstructed in such a manner that « there is a new strong, functional level when they already can quite cope with demands showed to an organism ».

Thus, a condition of successful professional work begins skill to be reconstructed with the count of sharp change of socioeconomic attitudes, valuable orientations, zoetic philosophy. But adaptation to varying conditions of professional work can optimum accomplish by constant adaptation of a professional knowledge through system of improvement of professional skill of teachers. Therefore as if the teacher further will be focused only on transfer of knowledge, skills, skills acquired by him the young generation inevitably appears unprepared to new situations which cannot be provided during any learning.

TEACHING OF CLINICAL DISCIPLINES IN MEDICAL HIGH SCHOOL AT THE PRESENT STAGE

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Steady growth of Scientific and Technical Progress, Pedagogical Science advances as a whole and Higher School in particular, make using of their achievements necessary in the process of teaching at Clinical Departments of Medical Higher Schools as well. According to our experience, optimal learning results are possible to be achieved when observing the following algorithm of teaching senior students.

1. Individual extracurricular self-development (studying special textbooks, scientific and didactic literature)
2. Self-development control, when the teacher pays attention to possible omissions, basic, most meaningful and most complicated questions of the studied problem. It is important that explanation words were proved with the demonstration of visual, simple and easy to memorize material. In the academic process at our Department of Childhood Surgical Pathology, topical video-films', available table and slide materials' demonstrations are used; modern computer multimedia and animation technologies of teaching provoke great interest. The given forms of distance teaching serve as an essential addition to "at-the-couch-of-patient-education", but never should substitute it.
3. Topical patients' medical supervision is made up in the form of a role game, when a student gets an opportunity to find out clinical stigmas of this or that disease on practice and to study the materials of a certain patient's laboratory and instrumental examination. For the correct interpretation of the data got we try to stimulate their being discussed among the students (discussions in micro-groups), that is obligatory to be finished with the teacher's discussion of the given clinicodiagnostic situation.
4. Medical duty experience of students with their department's teachers in emergency cases, students' development of necessary practical skills and competence are impossible to overstress, as they watch and take part not only in solving urgent tactical and practical tasks, but also often solve ethic, deontological and moral problems with assistance lecturers and lecturers of their department, involuntarily adopting the best personal features of their teachers.

The denoted above principles of the team-work of a teacher and students are the most important components of training of Medical Higher Schools' senior students, as such a model is able to reproduce the experience of future doctors' professional and personal development.

THE TRANSFORMING POTENTIAL OF GLOBAL LEARNING ENVIRONMENTS: A CASE FOR GLOBAL SEMINAR PROJECTS

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Globalization has forced education to explore new practices designed to help educational systems meet the demands of a fast changing world economy, increasingly globalized culture, and rapidly growing interdependency of human societies. Striving to build and maintain a global system of educational institutions, educational researchers and administrators worldwide have started developing and implementing in practice a concept of "global education." Scholars view this concept separately from globalization, as a construct that aims to extend students' awareness of the world in which they live by opening them to the diverse heritage of human thought, action, and creativity (Sterling, 2001). The interdisciplinary field of "global education" emerged from various areas of academic discourse, such as international relations, cultural studies, environmental studies, and economics (Kirkwood , 2001; Lamy 1987),

and during the last decade of educational research it has come to be seen in greater and greater clarity.

Applying the concept of "global education" to higher education has led to strategic rethinking modeled on the perceived demands of globalization to improve educational effectiveness and connectedness and to produce the "global graduate," a student with competencies in scholarship, lifelong learning, and global citizenship, a person who will "aspire to contribute to society in a full and meaningful way through their roles as members of local, national and global communities." [Graduate Attributes Project].

In line with these trends in "global education," many universities have developed policy frameworks that include the expectation that college students will develop the broad range of intellectual and social skills necessary to the acquisition of global competencies. Today, all modern universities have strategic plans that reflect the overall educational system's movement towards globalization in practice and in student requirements and expectations including lists of student attributes, goals, and acquirements associated with "global citizenship." Curriculum committees and university faculty use these strategic documents as guidelines to develop and implement practices that promote global learning in the college classroom. North American educators in particular have striven to do this in various ways, one of which is to create undergraduate and graduate courses sympathetic to and constructive of "global learning environments.

Global Learning Environments

The "learning environment," conceptually a fairly recent phenomenon, would seem not to be particularly well substantiated by a large body of underlying educational theories. In North America, research on "learning environments" has its roots in educational psychology and builds upon instructional theory promoting the latest technological advances in education and studying the impact of its effects on students' learning. Coerced by a globalized information economy powered by internet-based communications, universities create virtual courses that provide cases for research on such subjects as "communities of learners," "global villages," "electronic learning environments," and "virtual universities." Most research on learning environments is performed in business settings, and it examines issues related to learning in terms of successful collaborative efforts. Fewer studies have been made of internet-supported courses, and these focus primarily on student satisfaction with the course rather than with learning outcomes. In my own research I focused my attention on a distinguished university, examining unique global features of a single learning environment with the intention of defining the potential of global learning environments in terms of educational transformation and the possibilities of promoting change in higher education.

I focused my research on the "Global Seminar Project" (GSP), an ongoing international collaborative program that offers to undergraduate and graduate students around the world an academic credit course on the central theme of environment and sustainability. Assuming that most of the teaching and learning principles that apply to traditional classroom course design apply as well to global learning environments, I interviewed twenty course instructors at their annual international meeting in Arlington, Virginia (USA), in July 2005. By interviewing the course instructors, I determined an order of factors, course design features, and course activities that together allowed the GSP participants to create and maintain the course's global perspective. Using ATLAS software to uncover the underlying content of these interviews, I determined that the GSP global environment consisted of six clustered items: conducive course content, stakeholder involvement, institutional support, course structure, course management (facilitation and academic leadership), and teaching and learning practices. These items comprise collectively the conditions required for bringing about and for sustaining the global learning environment.

GSP global potential: possibilities for transforming education

My interest in the transformative power of a "global learning environment" has been guided by the transformative educational system frameworks of Mesirov and Sterling (Mezirov, 2000; Sterling, 2001). Examining the aspects of GLE with these frameworks in mind, I came to appreciate each GLE feature as transformative, constructive, and participatory in style, structure,

management, and content. From this perspective, the transformative nature of the GLE can be viewed as an alignment of all of the elements of the GLE model. This understanding led me to think that facilitating global learning environments in university settings for particular purposes might indeed provide a compelling model for transforming higher education practices generally in support of "global learning." To place this understanding in a framework of "global education" I defined GLE as an approach to education with the potential to initiate transformative changes in educational systems consistent with the requirements of a globalized world economy. The GLE is a process emphasizing educational and social values related to quality of process, development of student potential and autonomy, equality of opportunities, community connectedness, and social constancy. It uses a "managerial" approach (Sterling, 2001) to realize economic values in education, such as efficiency and quality control. It can be viewed both as an approach and as a process for educational transformation, providing opportunities for global collaboration and learning for faculty, administrators, and students, encouraging and facilitating dialogue among the major actors and stakeholders with regards to and in the area of global issues, and bringing new perspectives to the promotion of transformative changes in global educational systems.

Conclusion

The initial inquiry into the incidence and characteristics of the GSP global learning environment revealed evidence that the GLE consists of six essential features: conducive course content, stakeholder involvement, institutional support, course structure, course management (facilitation and academic leadership), and teaching and learning practices. These items comprise conditions for bringing about and sustaining the global nature of educational environments. Together, these elements generate possibilities for a sustainable, transformative change in higher education by keeping its focus on educational and social values while following economic, "managerial" values in its operations. As an approach and a process, GLE provides new insights into how to realize globalization effects in education and suggests new opportunities for a sustainable change in global educational systems. Because of the GLE

structural and operational complexity and qualitative nature of much of the research, it is difficult to make specific, long range recommendations. Some ideas for an immediate follow up might include:

- Recognizing the necessity for developing a solid conceptual base for newly emergent educational practices that might, on a global scale, not only indicate but also cause changes in educational systems affecting overall globalization processes;

- Acquiring information on changes in educational systems in relation to "global education" with respect to existing knowledge and practices that might lead to re-orienting education as a whole towards a more sustainable model.

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STUDENTS' CREATIVE GROUPS AS A DEVELOPMENT FACTOR OF INNOVATION POTENTIAL OF MODERN HIGH SCHOOL

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Modern system of Higher Education is characterized by complicated transformation processes that are the subject of theoretical reflection for many scientists and researchers. We observe the following dynamic trend in defining the priorities of its functions- from taking High School as an educational establishment concentrated on educational activities with operating center consisting of one-dimensional complex of multi-level educational programs (specialities, profiles and degrees) to providing high quality education based on scientific research and rendered by the academic stuff. Scientific research is not only an additional tool of performing the studying process, but is also a product of high school activity resulted in some kind of scientific knowledge, or technologies which can potentially produce a profitable effect on the market of innovations if to perform it rationally and correctly. Operating center becomes two dimensional (academic education-scientific research) where servicing component concentrated on implementation, dissemination and commercialization of knowledge and technologies occupies more and more important position. In process of transition to research type of high school, it requires special institutional representing and interpretation. It has the tendency to transit into separate institutional substructure, within which specialists but not the innovators would be responsible for implementation and getting social and commercial effect. Logically, a new technological subsystem appears and takes the form of different services of various types and levels.

Besides that, actual needs and requirements of the market of educational services make high school, on the one hand, follow the requirements of customer-oriented principle, offer new educational products in form of programs for intensive learning, distant courses, special products in the form of on-line resources, presentations, summaries, abstracts, supplementary materials of some topics and issues for self-learning by students, advisory services, combined and additional courses. On the other hand, high school should not only consider issues in sphere of education but also refer to the actual needs of industry and business and take them as a possible way of implementing its new products and getting orders for its further development. Adoption and financing of Federal Programs and also analytical program «Development of the scientific potential of High School (2006-2008)» give important contribution to that. Practical realization of such projects is impossible without scientific and methodological assistance of scientific and research institutional organizations and intellectual potential of high school.

Thus, in modern educational situation high school is oriented on different markets that mean one more aspect of consideration- the market one. The same idea is relevant to the scientific activities of high school. Work on the commercialization of technologies leads to different types of scientific products based on some scientific trend and accordingly to different ways of grouping scientists into spin off companies, creative theoretical groups, working research teams, groups on training school leavers, whose work does not necessarily follow the standards of the university courses. So, keeping to the traditional functional hierarchy of university departmentalization, serving «traditional» academic process, a lot of additional structures have been forming spontaneously in high school and help to realize the increasing number of new products of university activities. These structures do not correspond to the hierarchy of vertical functional departmentalization because they are horizontal schemes, combining the stuff of traditional subdivisions.

Nowadays the concept and educational technologies of training specialists have been changing completely. In their professional environment they have to solve complicated tasks, acting in the situation of uncertainty. In process of academic learning students should be focused on continuous professional and personal self-improvement, transformation the personality

for solving more sophisticated creative tasks of any professional activity.

Our modern economic life defines new innovative ideas required by the society and the acute need in innovative and active specialists with university degrees. We consider innovative activity as an inseparable characteristic of a specialist with university degree. So the main purpose of any higher educational establishment is bringing up innovative and active personality, ready for effective functioning in modern economic conditions and having new ideas and approaches for professional and social problem solving.

Having analyzed the theoretical approaches described in the scientific and pedagogical literature and models of modern academic practices on acquiring students the experience of innovative activity in process of professional training; we have come to a conclusion that today we do not have effective mechanisms for exposure innovative students and using the potential of student's creative groups. Traditionally problems of forming student's creative activity are interpreted in context of simulated situations which the students might face up with and their involvement into collective research practice by using given knowledge in the mode of quazi-professional activities imitating essential and technological aspects of their future profession. Problems concerning organizational conditions for bringing up innovative and active personality in the educational environment of high school have not been theoretically worked out. Today there is a necessity of designing methodological, social, psychological and institutional principles on using personal potential, personal development and bringing up of innovative specialists in higher educational establishment.

The conceptual approach to the problem of increasing innovative activities of students in high school designed while working on the research project « Cluster application as methodological principle of stimulating innovative activity of students» and analytical program « Development of scientific potential of high school (2006-2008) » supposes complex measures on forming innovative and active student groups effectively cooperating for creative solving of technical business orders. One

of the components of this system is the creation of new institutional structures.

The functions of this structure include:
- realization of combined organizational methods and procedures, necessary for creation innovative and active environment in higher educational establishment,
- designing the optimal strategy of stimulating innovative activity of every participant of educational process, mostly students,
- monitoring all tendencies and regulating the whole activity on the creation of innovative educational environment of higher educational establishment.

The main tasks of this organizational structure include:
- identification and dissemination of innovations that academic workers actively apply in their practical activities,
- organization of purposeful people activity, cooperating for the realization of innovative idea, implementing it and getting economic profits,
- commercialization of the results and solutions on the base of economic potential of the idea,
- optimization of educational process in high school by applying principally new scientific, methodological, managerial, organizational and other decisions,
- creation of cross disciplinary and interdepartmental subdivisions which would appear as the decision-making centers for the realization of innovative ideas on certain problems,
- mobilization of various high school resources for realization of innovations in sphere of educational activity,
- specialist training on resources mobilization for effective implementation of innovative process in high school.

Functioning of this institutional structure should promote complex development of all subdivisions in high school providing commercialization of the results of innovative activity, bringing up and positioning leaders who are able to initiate and manage innovations, organizing highly qualified specialist teams to work in sphere of innovation.

According to the modern requirements one of the main tasks of effective functioning of the

described structure is training consultants on mobilization resources for implementing innovative activities in every sphere. In foreign terminology they are called «innovative consultant» or «catalyst». The number of these consultants is the criteria of innovative activity of not only a certain organization but also a country.

The most valuable part of consultants' activity is their assistance in increasing innovation potential, which is the ability to percept and effectively use innovations, to create problem-oriented expertise systems aimed at modeling future specialists behavior in innovation decision-making, to prepare intensive technologies for innovation design. Interrelated contacts and behavioral patterns within innovation groups become its inner content in process of professional growth. Specific self organization that accompanies the process of group cooperation becomes the «mechanism» of forming personal educational environment of each group member where he acts as a subject of his personal development and at the same time as the agent of innovation in modern high school.

Shot report

INFORMATION MODELS OF ADDICTIONAL GROUP BEHAVIOR

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Some original search results of differential analysis of narcoepidemiological processes and other social psychology knowledge are compared and studied. The ideology of the information modeling as universal method into social ecology, psychology, narcology, epidemiology and human biology is described. It contains some original theoretical-games models of the human population behaviour, self-organization and adaptation in social extreme events, as well as methodology system analysis of criminology influence on the psychological state of human population. At the group behavior study on RHSF grant № 05-06-06098a «Information modeling of group dependencies of consumers of drugs» is used information (strategic) modeling method in combination with the instrument of applied conflictology. Created formal group dependency models in the manner of coalition games for *N* persons, tend to the satisfaction of individual and group need. Build models of group and intergroup behaviour of organized criminal groups with using a mathematical device of modern game theory. Shown that by means of the proposed approach is possible sufficiently detailed to describe the pack outline is social-psychological objects and processes, meet in real problems of demography and criminology, not having hitherto identical formal description. Incorporated mathematical objects - layered deterministic and stochastic cooperative and coalition games and their associations, corresponding to problems of finding of optimum deciding for modeling systems. Incorporated functions of advantage, reflect destroy/restoring influence on under investigation system parameters. Build procedure of narrowing an ensemble of strategies, acceptable from standpoints of conservation of acceptable system development. We research class of layered games as a device of complex hierarchical criminal system modeling. Offered and are explored layered games and their expansion, assign by ensembles of interests of players and coalitions. Formed games, forming formal base of models an economy-criminology systems, are found condition reality and the existance of optimum deciding build descriptive models. Class study of matrix games has prove the existance of exact algorithm of deciding, herewith to the account of entering the pre-strategies manages real to describe events of entering the players simultaneously in different coalitions. Game-theoretical concepts allow correct to prototype behavioral and communication processes in transcultural and ethnics groups, regularities of their origin, developments and involvement of new participants. Explored information models of collective flow of consciousness beside representatives of different informal groups of teenagers. Criminology study have show that important particularity criminal groups in the sphere of the illegal turn of narcotics is a high level an autocontrol, vitality and stability of hierarchical group structure (more than 3 sections), complex functional relationships between levels and clear sharing the duties between all group participants. Strategic models of group behavior of consumers of narcotics are checked also on material narcoepidemiology, social-psychological and ethnocultural studies.

SOCIAL AND ECONOMIC CONDITIONS OF REFORMING OF EDUCATION IN THE REGIONS OF THE EAST SIBERIA AT THE TURN OF XX AND XXI CENTURIES

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The communication between the processes of reforming of the public education in the East Siberia at the turn of XX and XXI centuries and its social and economic background are analyzed in this article.

Now modern Russia is at the special period of its history, which characterized by the radical social and economic rebuild of all the sides of social life. In general its main idea mostly defines as a market economy and market economic relations. As the professor A.N. Falaleev considers, there is no full coincidence with the character of those reformations which occurred for example in Russia and in the other countries at the end of XIX - beginning of XX centuries, and it should not be if for no other reason than for the last century the world order suffered the most important changes [5, P.3]. However, it is possible to say about some aspects, which characterize the analogy of the periods of the history of Russia at the end of XIX and the beginning of XX centuries and the end of XX – beginning XXI centuries, that the development of market economy, the domination of private property, reforming of different spheres of social life, including the field of education. The period of the end of XX and the beginning of XXI century is also characterized by the transition to market economy. The national property was changed by the other numerous forms such as: private, federal, municipal (according to the Constitution), and that has defined the diversification of the forms of education, as at the end of XIX and the beginning of XX centuries as at present. There is every

indication that there is an affinity between the educational problems of both periods.

At the period of the end XIX and the beginning of XX centuries the development of the native school is always the focus of attention of the scientists. This comes from the uniqueness of its experience unicity, bold ideas and the projects of the founders of the end of XIX - beginning of XX centuries.

But it is necessary to mark that in the historical and pedagogical literature the questions of the public education are mostly went into the question at large in the context of the reforms taking place in the center of the country and in the regions – the question of realization was far less touched on. This is not enough for drawing up an overall picture of the national education development. Thereby the processes in the education of the Russian Regions are of a great interest. To give the low-down on the history of Russia and the national education on the whole it is necessary to find out the regional features, which influence on the reforming process in all spheres of life in Russia at the end of XIX - beginning of XX centuries.

As a result of the reforms in 1864 in Russia the land reforms were carried out, and it introduced the District Council Election all over the central part of the State. These Zemstva (elective district councils in the pre-revolutionary Russia) took the lead in the development of political, economic and

social condition (situation) of the citizens of Russia, created various mutual aid societies, loan offices, and opened numerous schools and so on. In the East Siberia, including the Irkutsk General-Governorship (the Irkutsk and Yenisei provinces), Yakutsk and Trans-Baikal provinces, the Tsarist Government, considering the East Siberia to be a colony, put obstacles on the way of the reforms, and explained that by the originality of social, economic and demographic factors until the beginning of XX century. As O.Yu. Seichenko notes in his work that the question of putting the Zemstva in force and of the social and economic conditions in the society had been taking place during all the second period of XIX - beginning XX centuries" [4]. The Zemstva were given a right to decide a question of the public education mainly in regard of economics. But the Zemstva were included into the process of the national education in the several directions: the organization of schools in the countryside, the determining of the optimal type of schools, according to the local needs and facilities, teacher's training. Just the Zemstva were interested in a serious organization of schools, because they saw there a training of future specialists in different spheres of life. In this connection the assignment of the Zemstva for the development of the national education were much more than for the education in that region which had not any Zemstvo, that is the Yenisei province.

This problem was discussed by the Yenisei Council and Principal Committee on the needs of the agricultural industry in 1903. The Committee raised a question of the agriculture and also the education in the Yenisei Province. A peasant of the Minusinsk Uyezd (District) A.V.Orochko mentioned in his report a "poor training of teachers". Then the author of the article said that "the only advantage of the national education in our region is that it doesn't cost much for the Treasury" [2, P. 266]. In 1903 the Ministry of the public education assigned 7085 rubles, the department of religious affairs – 4000 rubles, the total sum was 11085 rubles, the rest was paid by the population. 11 000 rubles made up 4% of all the profit including the natural duty. The territorial provinces spent 20% and 30% of profit for the education [2, P. 266-267]. A.V.Orochko noted there was no body in the Yenisei Province responsible for the development of the national education.

Thus this can be explained mostly by the lack of Zemstva in the East Siberia. The problem of Zemstva's administrating in the East Siberia were lightened in the works of M.I.Altshuller called "Zemstvo in Siberia", A.A.Kornilov «A question of Zemostvo organizing in Siberia until the Imperial Rescriptum of the 3 of April in 1905. N.S.Yurtsovskiy «Zemstvo in Siberia» [3, P.20-89]. It is said in these works that the introduction of the Zemstva in the East Siberia let to improve the economy of the backward regions of the Russian Empire. Not only the economical backward of Siberia troubled the progressive political figures of Russia, but also the social and political aspect of the struggle for the implementation of the Zemstva. M.N.Yadrintsev contemporary with these events wrote: «Our first and urgent needs are the implementation of the Zemstvo, Public Court, freedom of the press and speech, individual liberty and security of property, ability to migrate and stop of banishment to Siberia». [6, P. 447] For this reason there was a backward in the sphere of the national education in the East Siberia, mainly in the Yenisei Province: "besides the special funds, sums paid for study, it is hardly to name any material resources to provide the teachers' training… because there is no Zemstvo in Siberia, the local community is not to be expected to do this; in any case they have not enough means to satisfy daily needs" [1].

The problems discussed in the article are also urgent for the modern economic and educational climate: the structural reorganization of the control on the spheres of social life, the problems of financing of

the education that is connected with the separation of powers in the field of the Federal, Regional and Municipal Authorities. The success of the educational reforming depends on the budget well-being of one or another Region. The effectiveness of problem solving of economic and cultural development in the Regions will increase by the realization of the objective government program in various spheres of life including the Education.

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Materials of the Conferences

MULTIWAVE LIDAR MEASURMENTS OF INDUSTRIAL AEROSOL EMISSIONS' CALCULATING AND MASS CONCENTRATION

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General atmosphere pollution increase and associated with it global changes of noosphere, energy balance in the Atmosphere-Earth system in peculiar, proved the actuality of applied fundamental research of chemical and physical properties and the structure of atmospheric aerosols and quantitative assessment of their role in the above mentioned processes. The aim of the research is the development of a method of estimation of different industrial enterprises' contribution to general pollution of the atmosphere over the territory of a large urban settlement. Meeting the goal objective was carried out on the basis of triple-wave ($\lambda = 1064$, 532 and 355 nm; laser radiation pulse duration on the 0,5 level is $\tau \leq 15\text{-}17$ ns.; angular spread of laser ray in the 0,5 level doesn't exceed $\theta \leq 2$ ang. min) and polarizing laser sounding of visually observable aerosol plume at different distances from the mouth of the corresponding tubes which were from 50 to 100 m tall [1]. Lidar measurements were carried out in Belgorod in 2004-2006 years in the location unit of a range of enterprises connected with concrete production. The lidar was located at a distance not less than 2 km from the enterprises. The quantitative assessments of aerosol masses' integral parameters (volume density V [мсм^3/см^3], typical radius of the particle r_{32} [мсм] and specific surface area S [мкм^2/см^3]) were carried out by means of solving an inverse problem of aerosol optics on the data about the size of measured visual thickness of these masses for dry and damp dust condition (refraction index of n=1,55 – 0.005i, n=1,41 – 0.002i accordingly). The analysis of the results of the triple-wave subflow sounding of the aerosol (under the lower edge of the visually observable flow) shows that the typical particles' size r_{32} assessment varies from 0,6 to 1,3 mcm. It is in an adequate agreement with the results of the carried out direct microscopic measurements of the typical sizes of the particles of dust in the selected from the last aerosol filter test samples [1]. The estimation of trickling aerosol percentage in the industrial emissions was carried out by means of additional use of polarizing sounding indication for the three typical cases: clean atmosphere, visually observable aerosol flow coming out of the tube mouth and aerosol "mark" under the flow. The back scatter indications $P_\parallel$ (with the polarization parallel to the origin one) and $P_\perp$ (with the polarization orthogonal to the origin one) in relative units and also the magnitude of the depolarization degree indication of back scattering $d = P_\perp / P_\parallel$ were subject to the analysis. It was experimentally proved that in the centre of visually observable flow the aerosol represents, in general, condensed steam. Under the visually observed flow the polarizing sounding indicates the aerosol consisting of nonspherical particles of concrete dust. These results are typical of many measurements of depolarization degree of a solid aerosol and adequately agree with the results of test measurements d for concrete dust.

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ENVIRONMENTALLY SAFE SCALE RESIST METHOD TO PROTECT BOILER AND WATER HEATING EQUIPMENT IN HEATING SYSTEM

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Rational use of fuel and power resources depends much upon the heat using efficiency in

all stages of its production, transportation and consumption. An important element in this sequence is its early stage connected with heat transfer from the burning heat-carrying agent (coal, gas, oil fuel) to the water which flows through boiler heating pipes. A great negative influence upon this process is exerted by boiler heating pipes' lime scale deposits.

It is stated that a 1mm thick scale deposit reduces heat transfer from the heating agent to the water 4-7 times as much, that leads to a great waste of fuel. That is why the problem of boiler and water heating equipment protection from scale is one of the most important ones. Traditionally it is being solved by means of softening or demineralization of water delivered to heating system charge. To do it water-preparing plants, the main purpose of which is the disposal of calcium and magnesium positive ions, which are the main scale-forming substances, from the makeup water, are installed in boiler houses. However, in some boiler houses water-preparing plants work not sufficiently enough, and in the other ones, especially those of low-power, there are often no such facilities at all.

The boiler and water-heating equipment protection from lime scale deposits can be achieved by using nonchemical methods of internal water treatment, that means the water is exposed to magnetic, ultrasonic and electric fields. These methods don't need bulky structures or special labs, don't use chemical agents. As a result, the formation of unusable waste and sewage, and water contamination are excluded. Besides, the ecological safety of heat-power engineering enterprises increases.

While being treated with a magnetic field, water flows through an interpole space perpendicular to the magnetic force lines, physical and chemical properties of the water being changed. Such changes occur in the water rich in scale-forming substances if ferromagnetic black iron oxide is present. In the water treated with a magnetic field its hardness doesn't change, but the pattern of solid particles solids' precipitation becomes different: the crystallization occurs not on the heat surface, but in the water mass with finely dispersed sludge formation [1].

When affecting the processes of scale-formation occurring in the boiler and water heating equipment with an ultrasonic acoustic field, special effects conditioned by the vibratory action of the metal surface and scale happen in the aqueous medium:

- the crystallization process is broken, due to what fine particles' aggregation with secondary scale formation takes place in the aqueous phase;
- the bond strength between the formed scale and the metal decreases, that leads to water penetration into the interlayer between the crust and the metal surface, to the formation of steam under the pressure of which crust lifting and flaking occurs;
- the disintegration of coarse particles of the hard phase which are formed as the result of crust lifting occurs.

Finally, the ultrasonic influence, as well as the magnetic field's one, on the processes of incrustation leads to the formation of secondary sludge, which has to be ejected by means of blowoff of the heating system in places of its maximal accumulation. The necessity of sludge ejection from the heating grid by means of its blowoff is the main disadvantage of intraboiler system water treatment with magnetic and ultrasonic fields.

There is no such disadvantage in the method of intraboiler water treatment with constant electric field [3]. The matter of this method is in the fact that the water flow containing dissolved, solid and also colloidal scale-forming substances is conducted between two inert electrodes onto which direct current flow is delivered. In the space between the electrodes an electric field develops under the influence of which physical and chemical processes proceed in the moving water flow. As a result of these processes solid and colloid particles of calcium carbonate and magnesium hydroxide pass from the water flow to the cathodes and settle out in terms of loose deposit.

The advantages of water treatment with an electric field are:

- high efficiency of boiler and water heating equipment protection from lime scale;
- lacking of limitations on mineral and carbon dioxide compositions of the water treated;
- insignificant energy demands and maintenance expenditures;
- easy servicing of the installation.

Antiscale apparatus represents a horizontal hermetic reservoir in which a system of electrodes is installed. The shell and the cathodes are made of carbon steel, the anodes – of graphite. The electric current is delivered to the electrodes from the constant current source. Regularly, the apparatus stopping, the cathodes cleansing from scale-forming substances' deposit and the ejection of it from the apparatus are carried out. The apparatus is installed in the heating and hot water supply systems before system water transmission to a boiler or water heater.

In Kuzbass State Technical University (Kemerovo) antiscale apparatus constructions of various capabilities are elaborated and unified. Technical characteristics of antiscale apparatus:
- Productivity, m/h………………...50-300
- Diameter, mm……………………800-1600
- Working pressure, kgsec/cm^2…….upto 8
- Working temperature, °C……..…..20-90
- Voltage on the electrodes, V…… .5-15
- Power consumed, kW/h… ……....0,1-1,5

The antiscale apparatus have been successfully exploited since 1987 in a range of boiler houses of Kemerovo Region. The exploitation results showed that their inculcation in heating systems increases inceasing working time of water heating boilers and water heaters by 3-5 times, reduces expenditures on heat exchange equipment cleansing and considerably solves the problems connected with waste recycling.

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Shot report

ECOLOGICAL HOMEORHESIS AS THE STAGE OF MICROEVOLUTION

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Homeostasis as relatively dynamic constancy of organism internal environment is evolving under the influence of extreme natural and artificial factors, the moving of a population to extreme climatic zones, the introduction of new species of organic origin into biocenose, the formation and the infill of ecological niches. We are working out the concept of ecological homeorhesis in terms of bringing it to line with ecological factors of homeostasis system on the level of population, species and interspecific.

Ingenious Ch.Darvin [1] ascertained fundamental regularities of evolution process, i.e. natural selection, working for the sources of numerous hereditary differences, existent in nature.

As is often the case in science, every prominent discovery in the sphere of evolution theory uncover the depths of our ignorance. This was marked since the 1920-s when it was shown that a population is an elementary evolution unit. At the end of 1930-s the basic theses on modern microevolution theory had been formulated. Next steps of ignorance were discovered in the 1960-s in connection with the development of genetic bases of evolution [2,3,4]. Geneticists-populationists started from argumentation of evolution of separate alleles (genes) and were made certain of insufficiency of such approach, came to the necessity to study the evolution of whole gene systems [5]. And, at last in the beginning of the XXI-st century we formulated the principle of microevolution by the first time. It is based on ecological homeorhesis as associating with ecological factors of homeostasis systems on populational, specific and interspecific levels [6,7,8,9,10].

The basis of the research is the system approach. The system is the aggregate of some elements, connected with one another and regarded as a single whole in terms of function and structure [11,12]. The system

microorganism- macroorganism is adaptive, i.e. it automatically changes function algorithms and/or the structure for achieving optimal state under the changes in the environment. In the given case both macroorganism and microorganism (virus) can be considered as components of adaptive system.

In natural scientific terms the macroorganism - microorganism system presents one piece with its elements being contrasts. The functioning of the system in biocenose is provided by the mechanism of distributing microorganism in the population of macroorganism [7]. The influence of the elements of the system is manifested as a struggle of opposites. As a result the whole system disappears or its components survive, being transformed or the adaptation of system components evolves (for instance, selection of naturally unreceptive populations of microorganism or naturally impaired populations of pathogen). This state should be examined as the stage of microevolution in system components or in the whole system with the formation of ecological homeorhesis in the macroorganism - microorganism system [9].

Starting mechanism in the formation of ecological homeorhesis is ecological stress [6]. It attributes to the impact of natural and artificial cataclysms, the moving to extreme territories, the introduction of new organic specimen into biocenose, the formation and filling of ecological niches. Ecological stress of different intensity can be acute (short-term and interchangeable with relative comfort) and chronic (long-term).

All kinds of stress lead to the development of different dysregulation processes, aimed at the transformation of existing homeostasis. In this respect the dysregulation of functions presents typical pathological process. These disturbances are transitory. They disappear after the elimination of pathological process and do not serve as dysregulation pathology. The last one represents the malfunction in organs and systems, which by itself becomes the reason of pathology development. Dysregulation can appear on all structural functional levels, starting with molecular, genetic, and completing with high relationships in biosystem [13] and system (mother – placenta - fetus, microorganism -

microorganism). But, reserved character of hereditary variability caused by recessive character of mutation relative to normal form of a gene does not allow fairly interrelate genotype and phenotypic manifestations [14].

In the process of the evolution of macroorganism - microorganism system the virus genes bear a resemblance to master genes. This makes easier virus reproduction or the completion of its life cycle (virus mimicry). It was ascertained that genes in the rank of viruses (Herpesviridae, Adenoviridae, Poxviridae) encode albumen, used by viruses to resist immune reactions of an organisms [15].

In high latitudes severe ecological factors influence all types of metabolism in humans [16]. This is reflected in the chemical content of internal environment (blood). An organism turns to the new level of homeostasis, which is characterized by the formation of new ecological norms of its health. On the populational level the systems of homeostasis are brought to conformity with ecological factors. The peculiarity of these changes is higher implementation of fats and lower of carbohydrates for energy needs. The role of albumen in energy metabolism noticeably grows. The need for water- and fat- soluble vitamins changes. These changes can be regarded as the development of polar (diametrically opposed) metabolic type [17] on populational level, which represents the stage in microevolution.

The association of small and large mammals provides the circulation of viruses of vernal encephalitis group under natural conditions of infection. It was determined that, the mammals are not ill with these diseases, including omsk hemorrhagic fever, including musk-rat. The animals develop virusemia, high enough to support epizootic chain. Viruses do not penetrate through hematoencephalic barrier into target organs, i.e. spinal cord and brain. In cases when they penetrate into, their reproduction is very limited and is insufficient for the development of the disease and the death of an animal. So, in epizootic chain, the provision of virus reproduction takes place as well as its preservation like species without the development of disease. In Siberia a musk-rat became an alien animal, being brought here from the USA in the 1930 – s and introduced into Siberia biocenose as a new ecological component. In the territory, previously inhabited

by the musk-rat, the virus of omsk hemorrhagic fever didn't circulate. In the terms of evolution an animal was not prepared to meet this pathogenic organism. In 1950 –s musk-rat epizootics led to the death of 92-95% population. Virulent virus was excreted from organs and tissues of spinal cord and brain in both diseased and frozen during winter dead musk-rats. In the 1960 – s nearly 50% of the musk-rat population died and in the 1970 –s in the period of epizootic, which we confirmed in the terms of virology, the death of only 4-6% of musk-rat population was registered. [19,20]. In the musk-rats, who were not ill, the virus was extracted from blood and inner organs. It was not found in spinal cord and brain or found very rarely and in low concentration [10, 20]. In hypodermic and intra-abdominal infection musk-rats didn't possess antibodies against omsk hemorrhagic fever and other stimulators of tick-borne encephalitis complex, virus strains, secreted in the 1950 – s, severe panencephalitis was developed in animals with the death at the 7-10 day after being infected. Musk-rats, infected extraneurally (hypodermically, intra-abdominally), through mouth and nose were dead 1-3 days later. In musk-rats, infected extraneurally by omsk hemorrhagic fever virus strains, extracted in the 1960–s, the outcomes were different. Some strains started the development of encephalitis with extremities paralysis and death of the animals. Others showed only inertia and in some cases slight convulsion. Many of musk-rats recovered [18, 20]. In musk-rats, infected extraneurally with virus strains, extracted from healthy musk-rats in the 1970 – s, as a rule, there were no cases of illness or death [10, 20].

In the past measles virus circulation in isolated human populations was utterly limited. 100 – 150 and more years ago when stimulator was brought to Russian Circumpolar territories, 50-95% infant and adult inhabitants got ill and died from measles. In 1947 with almost 100% morbidity (measles) in the Extreme North there were no mortal cases caused by this disease [21, 22]. From the 1950 – s and up to vaccination period the measles morbidity in high latitudes reached 1500-4000 per 100 000 subjects, i.e. it exceeded the morbidity in middle latitudes dozens of times. But at this time not a single mortal case was revealed. The cause of the disease was very light and with further recovery [23].

In year 2000 the infection diseases, which can be eliminated by vaccine prophylaxis, were the reasons of 1 700 000 infant deaths in the world. Among them diphtheria 0.2%, whooping-cough 17.3%, measles 45.5%, yellow fever 1.8%, Jlib-infection 23.4%. The analysis of measles morbidity shows the prevalence of fatal outcomes in tropical and subtropical zones in Afro-Asian continent, 60% of them taking place in Africa, i.e. in the area with the highest air temperatures, 30% in South Eastern Asia, 10% in the East Mediterranean part. Because of vaccinal prevention against measles in these regions from 1990 to 2001, the ratio between recovering and mortal cases in the group of diseased, non-inoculated subjects remained the same. In the Extreme North the clinical cause of measles infection was light not only in native, but in alien population as well. This proves lower virulence of a virus, which circulates in high latitudes.

It is known, that under natural conditions virus circulating strains consist of more of less virulent virions. Virus virulence is caused both by the receptivity of macroorganism and the ratio (virus strain) between virulent and naturally impaired virions in population. In the process of interaction between macroorganism and microorganism in population, the last one has definite advantages in the process of adaptation and selection, because its reproduction per time unit essentially surpasses the reproduction of macroorganism [24]. At the same time virulency and pathogenicity of microorganism is caused only by its preservation as species, which is determined by the ability to be distributed in population, population flow or microorganism body. The experience of creating living vaccines against poliomyelitis, measles, rubella, parotitis and others confirmed this statement. In tissue cultures under low temperatures (indication rct_{30}) vaccine, non-virulent for humans virus strains were selected. Highly virulent populations were selected under 40-42 degrees. Probably, air temperature became one of the factors, resulting in virus strain selection with different virulence. Air temperatures in the Extreme North are very low, at the same time face and upper nasopharynx part temperature is 2 degrees lower as compared to middle latitudes. We do not have the data on nasopharynx temperature in tropical and subtropical zones.

The analysis of the obtained materials allows to come to the conclusion that under extreme ecological conditions at the present time microevolution happens both in population and in the system of microorganism-macroorganism populations. Starting mechanism of ecological homeorhesis formation is ecological stress, which induces the development of different deregulatory processes (phenol- and genotypic modifications). Deregulation is malfunction of organs and systems, which leads to the dependence from the intensity and duration of ecological stress or to adaptation or to disadaptation. The last one on the population level can cause pathology in some representatives of population or to induce selection (natural or artificial) in others. When the evolving homeostasis comes into conformity with extreme ecological factors on the population level, ecological homeorhesis is being formed, which is the stage of microevolution.

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Materials of the Conferences

INTERNATIONAL RELATIONS IN MORDOVIAN STUDENTS' EVALUATIONS
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The aim of the head count held in December, 2005, was to define the attitude of student youth of Mordovia to the State National Policy. A hundred of Mordovian and a hundred of Russian 2-5-year students took part in the head count. The results you can see in the table.

Table 1. The students' evaluation of the state of international relations in Mordovia (in %)[*]

Questionnaire	Mordva	Russians
Are you satisfied with the National Policy in Mordovia in general?		
а) no doubt, and rather satisfied than not	48	46
б) no doubt, and rather not satisfied	30	37
Are national right s violated more often or seldom than in other regions?	25	32
а) rather and not so much often as seldom	39	40
б) no difference from the other Regions	9	9
в) rather and not so much seldom than often		
Who is responsible for the protection of national rights by all means?		
а) Federal Authorities	30	31
б) Regional Authorities	53	62
How do you value the state of international relations in Mordovia?		
а) good and very good	29	28
б) normal	66	61
в) bad and very bad	2	6
What are the reasons of tension in international relations?		
а) National Policy errors in Soviet period	13	14
б) present–day Federal Authorities' actions	2	3
в) Regional Authorities' actions	12	8
г) deterioration of economical situation	27	31
д) migrations from other Regions of the country	24	43
е) disrespect to the language and customs of people of different nationalities in every-day life	53	53
ж) purposeful discord fomentation by political groupings and the press	27	27
Have you faced recently:		
а) violence on nationalistic ground	29	31
б) prejudices relative to other Nationalities	32	31
в) cold-shoulder to people coming from other Regions	40	49
Do the Federal Authorities' actions help to solve these problems?		
а) they let them be solved as a whole	9	17
б) they are not performed by local authorities	18	14
в) the actions are late and are transformed into conflicts	16	29
г) they themselves are the reasons of the conflicts	10	12
д) it is difficult to say	44	26

Some questions require several variants of answers, only the most significant ones are mentioned in the table.

As a whole, more or less loyal attitude of Mordovian students both to representatives of other nationalities and to the policy conducted by the Federal and local authorities in the National Policy is marked. But never the less, more than a half of the respondents faced the facts of national disrespect in every-day life that necessitates keeping on working on culture of international relations and the development of tolerance.

Materials of the Conferences

BROWN ARID SOILS AND VEGETATION OF DRY STEPPE REGIONS IN DIFFERENT PASTURE REGIMES USAGE

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The calamitous state of dry steppe regions because of overgrazing like Aral region, Central Asia, North and Youth Turan, Black lands of Kalmykia and Tersko-Kumskaya lowland at the West Pre-Caspian depression ceased be news for the world scientific community long ago. In comparison with other natural zones under semi desert conditions there are simplified vegetation cover, weak accommodating possibilities to weather changes, weak reproduction, narrow diapason of environmental usage, less productivity and nourishment, higher vulnerability and variability degree under grazing. To restore the degraded arid pastures it is widely used the fodder grasses sowing, moderate grazing, forest belts cultivation, periodical regime of preservation of pasture territories.

The aim of this research is to give a generalized description of interdependency of vegetation and brown arid (light-chestnut) soils of the Tersko-Kumskaya lowland, which are the basic pastoral fund of region, in the regimes of preservation and grazing. Experiments were carried out since 1987 till 2006 year at three key zones in the scientific research framework of The Caspian Institute of Biological Resources. The first key zone is situated in the central part of Tersko-Kumskaya lowland: G1 – grazed ground 2-3 heads of sheep per hectare (h/ha), P1 – preservation regime during 3 years (0 h/ha). Soils are loamy sand solonchacovaty small massive. Vegetation represents stepped meadow composed by *Cynodon dactylon* with areas of *Camphorosma Lessingii, Atriplex tatarica, Suaeda microfilla, Ceratocarpus arenarius*. The second key zone is situated in the east part of the lowland. The regimes of grazing and preservation were studied in two repetitions: G2a – 3 h/ha, P2a – preservation regime during 4 years. Soils

are light loamy solonchacovaty medium massive. G2b – 4 h/ha and P2b – 2 years. Soils are light loamy solonchacovy small massive. The soils of the second key zone are formed under cereals-wormwood plant groups from *Artemisia taurica, Art. austriaca, Poa bulbosa, Camphorosma Lessingii, Kochia prostrata.* The third key zone is situated in the north-east part of the lowland, grazing (G3) – 2-3 h/ha. Regime of preservation was spent under artificially introduced and irrigated during 12 years with artesian water forest massif composed with *Ulmus pumila, Elaeagnus angustifolia, Robinia pseudoacacia, Ziziphes jujuba* (P3). The soils are loamy sand solonchakovy small massive. Vegetation is represented with cereals-wormwood plant groups from *Artemisia taurica, Art. austriaca, Atriplex tatarica, Camphorosma Lessingii, Kochia prostrata, Alhagi pseudoalhagi, Suaeda microfilla, Poa bulbosa, Agropyron desertorum, Polygonum aviculare.* The samples for key zones were picked out in the following order: 1 – august 1987; 2 – July 1992; 3 – May 2006.

Introduced regimes of preservation promoted to main physical and chemical characteristics changes in soil profiles. Temperature in the upper soil lay lowered by 1.5-2°C (P2a, P3); upper horizons became less dense: the volume weight in regime of preservation decreased – 1.35, 1.37 g/cm^3 (P3, P2a) in comparison with grazed pasture – 1.47, 1.5 g/cm^3 (G3, G2a), relative moisture decreased – 3.6 % (P3) against grazing regime – 5.5 % (G3), the soil surface deflation was slackened 2-4 times as much (P2b, P3). The regimes of preservation promote to soil profiles desalinization. Soil reserves in meter thicknesses of loamy sand soils are 28.37 t/ha (P1, P3) against 33, 72 t/ha (G1, G3). Due to leached soil meter thicknesses, the contrast of salinization degree of soil profiles decreased. On the soils with more heavy granulometric composition (light loam) only the upper 30 and 70-cm thicknesses was leached and in that case salts accumulated in lower soil horizons causing the increasing the contrast of degree salinization of soil profiles. Salt reserves in meter thicknesses of both regimes were practically the same: 113, 116 t/ha (G2a, P2a), 135, 143 t/ha (G2b, P2b).

The vegetation of preserved territories considerably changed: its ground, underground plant biomass (phytomass), projective cover. The ground phytomass productivity under forest massif (P3) increased up to 23 centners/ha (c/ha) with projective cover (PC) 90-100% because of cereals and forbs synusium with average plants height of grass layer 120 cm, while at the pasture (G3) the productivity was only 6 c/ha with PC 30-40 % (october 2004). In the forest belt lower grass layer vegetation cover diversity had grown: the areas of *Glycyrrhiza glabra, Phragmites communis, Agropyron desertorum, Polygonum aviculare, Convolvulus persicus* measuring 2-40 m^2 were registered there and they caused creating interfacial mosaic structure. Synusium changings of cereals and halophytic plants typical for semi desert vegetation were not observed in contrast to pasture. During 12 years there were formed forest landscape features: low layer consisted from cereal forbs, forest litter formed with deciduous and grass matter. The forest massif Fauna underwent changes too: lizards almost vanished, bugs were multiplied, crows nesting places appeared on trees. Thus we can speak about artificially introduced absolute original facies with its own characteristics. In the central part of region (first key zone) regime of preservation promoted to vegetation cover increasing from40-50% (G1) to 90-100 % (P1). Plant species structure was supplemented with *Phragmites communis*. While pressure became 4 sheep per ha (G2b) the following species such as *Stipa capillata*, *Koeleria cristata*, *Agropyron desertorum* disappeared, gradually abandoning herbage. Bad palatable *Artemisia Lerchiana*, *Poa bulbosa*, *Artemisia pauciflora, Atriplex tatarica, Polygonum aviculare* remained, and vegetation cover gradually degraded. Root matter underwent changes too. In regime P2a in the thickness 0-60 cm common root mass decreased up to 154 c/ha against G2a – 242 c/ha (august 1990); besides root mass quantity the structure of underground phytomass changed because of decreasing of rod roots (diameter >3 mm) from 13-29 % (G2a) to 5-8 % (P2a), in upper 0-20 cm layer roots >3 mm in P2a were absent. Thus, decreasing of rod roots quantity and participation became a reason of weakening of root suction, hence salt reserves decreased and relative moisture became lower in regime of preservation.

The analyze of brown arid soils and vegetation in different pasture regimes usage showed, that short-term regimes of preservation (in contrast to grazing regime) promoted to: desalinization of upper soil layers, changing of the contrast of salinization degree of soil profiles, weakening of soil deflation, lowering of temperature, decreasing of relative moisture because of root suction weakening, lessening of root mass quantity, vegetation cover augmentation, changing of plant species, changing of ground and underground phytomass structures. Generally, regimes of preservations on brown arid soils promoted to optimum state of soil processes and productivity restoration of pastures. Forest massif cultivation in addition to preserved regimes permited radically transform arid landscape to positive side up to creating of new landscape facies which is more autonomous to negative external influences.