Medical and Biological sciences

Articles

Materials of the Conferences

CONTENTS

IF YOU FEED THEM, THEY WILL COME: A PROSPECTIVE STUDY OF THE EFFECTS OF COMPLIMENTARY FOOD ON ATTENDANCE AND PHYSICIAN ATTITUDES AT MEDICAL GRAND ROUNDS AT AN ACADEMIC MEDICAL CENTER

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Evidence suggests that attendance at medical grand rounds at academic medical centers is waning. The present study examined whether attendance at medical grand rounds increased after providing complimentary food to attendees and also assessed attendee attitudes about complimentary food.

Methods: In this prospective, before-and-after study, attendance at medical grand rounds was monitored from September 25, 2002, to June 2, 2004, using head counts. With unrestricted industry (eg, pharmaceutical) financial support, complimentary food was provided to medical grand rounds attendees beginning June 4, 2003. Attendance was compared during the pre-complimentary food and complimentary food periods. Attitudes about the complimentary food were assessed with use of a survey administered to attendees at the conclusion of the study period.

The mean (± SD) overall attendance by head counts increased 38.4% from 184.1 ± 90.4 during the pre-complimentary food period to 254.8 ± 60.5 during the complimentary food period ($P < .001$). At the end of the study period, 70.1% of the attendee survey respondents indicated that they were more likely to attend grand rounds because of complimentary food, 53.6% indicated that their attendance increased as a result of complimentary food, and 53.1% indicated that their attendance would decrease if complimentary food was no longer provided. Notably, 80.3% indicated that food was not a distraction, and 81.7% disagreed that industry representatives had influence over medical grand rounds because of their financial support for the food.

Background

Medical grand rounds (MGR) is a central teaching activity in US departments of medicine at academic medical centers. However, attendance at MGR by faculty, fellows, and residents appears to be waning even though the perceived quality of MGR is increasing [1-3]. This decrease in attendance, coupled with the considerable resources (eg, financial resources and time) invested in this activity, should cause MGR planners and continuing medical education (CME) providers to question why attendance is waning.

Moore [4] described a 6-level approach for evaluating the value of CME. Each level is associated with an outcome: participation/attendance, satisfaction, learning, performance, patient health, and population health. The present study focuses on measuring attendance as an outcomes measure. On the basis of Moore's model, increasing attendance is a legitimate CME goal.

One commonly used strategy to increase attendance at MGR is to provide complimentary food [3]. Observational and anecdotal data indicate that complimentary food can increase attendance at meetings and educational events [3,5-8]. Notably, needs assessments at our institution identified lack of food as a barrier to attendance at MGR [2]. Complimentary food has also been associated with successful, well-attended internal medicine journal clubs [9].

Nevertheless, providing complimentary food requires substantial financial resources. However, before financial resources are allocated or sought from outside sources to provide free food, a study examining the effects of complimentary food on attendance at MGR should be undertaken. Attendee attitudes should also be assessed to evaluate

whether this intervention changes one's attitude toward MGR [8]. To date, no systematic study has examined whether complimentary food increases attendance at MGR or what effect complimentary food has on attendee attitudes toward MGR.

MGR at Mayo Clinic (Rochester, Minnesota) is a 1-hour, noontime, weekly conference sponsored by the Department of Internal Medicine (DOM). The main site for MGR is a large auditorium in the outpatient clinic facility, but the conference is telecast elsewhere on campus. At Mayo Clinic, the principal objective of MGR is to educate DOM faculty, fellows, residents, and students about advances in internal medicine practice, research, and education. Additional objectives of MGR are to provide opportunities for socialization and CME credit. These objectives are similar to those of MGR in departments of medicine elsewhere [1-3,10].

We report the results of a prospective, before-and-after study of the effects of providing complimentary food on attendance at MGR. We also report the results of a survey that assessed the attitudes of MGR attendees on the provision of complimentary food.

Methods

From September 25, 2002, to June 2, 2004, the attendance at MGR at Mayo Clinic (Rochester, Minnesota) was tracked by the use of head counts. During this period, food was available for purchase near the main auditorium and main telecast site. Beginning June 4, 2003, complimentary food was provided to MGR attendees at the main auditorium and at the main telecast site. The cost of the complimentary food was underwritten, in part, by an unrestricted grant from industry. Complimentary food included a sandwich, a piece of fruit, and a beverage. Attendance at MGR before complimentary food was provided was compared with attendance after complimentary food was provided. For data analysis, the periods were matched by week of the year because of possible seasonal variations that might affect attendance. Specifically, attendance at MGR during the pre-complimentary food period from September 25, 2002, (week 39 of 2002) to May 28, 2003, (week 22 of 2003) was compared with attendance at MGR during the complimentary food period from September 24, 2003, (week 39 of 2003) to June 2, 2004, (week 22 of 2004). Attendance counts were eliminated if attendance data were missing (eg, because of a holiday). Head count data were available for 29 corresponding weeks during the pre-complimentary food and complimentary food periods, for a total of 58 events in the analysis. Given the nonnormal distribution of the data, a Wilcoxon/Kruskal-Wallis test (rank sum test) was used to calculate *P* values. The level of significance was $P < .05$.

To assess the attitudes of MGR attendees about complimentary food, a Web-based survey was administered to 943 DOM faculty, fellows, and residents (See Appendix for the survey questions).

Group comparisons of survey response distributions were done using the Pearson χ^2 test. In cases of small cell counts, a hybrid Fisher exact test was used for the comparisons [11]. *P* values less than .05 were considered to be statistically significant. All analyses except the hybrid χ^2 analysis were conducted using JMP 5.1 software (SAS Institute, Inc, Cary, North Carolina). The hybrid χ^2 tests were run using a Fortran routine (The Fortran Company, Tucson, Arizona) on a UNIX platform (The Open Group, San Francisco, California) [12].

This study was approved by the Mayo Clinic Institutional Review Board.

Results

Effect of providing complimentary food on attendance at MGR

The mean (± SD) overall attendance increased 38.4% from 184.1 ± 90.4 per MGR session during the pre-com-plimentary food period to 254.8 ± 60.5 per MGR session during the complimentary food period ($P < .001$). Similar significant results were obtained when head count data for the main auditorium ($P < .001$) and the main telecast site ($P < .001$) were examined separately (Table 1). Notably, the size of the DOM increased by only 6% during the study period.

Complimentary food survey

After the study period, a Web-based survey was administered to all 943 DOM faculty, fellows, and residents. Of these, 444 (47.1%) responded (some respondents did not answer all questions; Tables 2, 3, 4, 5).

Table 1. Head Counts of Attendees at Medical Grand Rounds

Site	Head counts, average no. of attendees per MGR session*		
	Pre-complimentary food period	Complimentary food period	*P* value
Main auditorium	160.0 ± 81.6	208.6 ± 55.9	< .001
Telecast site	24.0 ± 12.5	46.2 ± 11.6	< .001
Total (both sites)	184.1 ± 90.4	254.8 ± 60.5	< .001

MGR, medical grand rounds.
* Mean ± SD.

In response to the question "On average, how frequently do you attend MGR?" a majority of respondents (67.4%) reported that they attended either weekly or monthly. The responses of faculty members to this question were significantly different from the responses of fellows (P = .034) and residents (P < .001). Specifically, fellows and residents indicated that they attended MGR more frequently than did the faculty (Table 2).

Table 2. Responses to the Question "On average, how frequently do you attend Medical Grand Rounds?"

Response	Respondents, %			
	Total* (*n* = 442)	Faculty†‡ (*n* = 261)	Fellow† (*n* = 74)	Resident‡ (*n* = 86)
Weekly	21.9	16.1	27.0	40.7
Monthly	45.5	42.5	50.0	50.0
4 to 6 times a year	28.1	35.6	18.9	9.3
1 to 2 times a year	3.8	5.0	2.7	0.0
Never	0.7	0.8	1.4	0.0

*Total includes respondents who were not physicians.
†Faculty vs fellows (*P* = .034).
‡Faculty vs residents (*P* < .001).

In response to the question "Are you more or less likely to attend MGR because of free food?" 70.1% of the respondents indicated that they were more likely to attend, whereas only 5.2% indicated that they were less likely to attend. The faculty's responses to this question differed significantly from the fellows' responses (*P* < .001) and the residents' responses (*P* < .001). For example, only 21.8% of the faculty respondents indicated that they were "much more likely" to attend MGR because of complimentary food, compared with 51.4% of the fellows and 44.2% of the residents (Table 3).

In response to the question "How has your attendance at MGR changed as a result of free food?" 53.6% of the respondents indicated that their attendance had increased, whereas 44.1% indicated that their attendance had not changed at all. The faculty's responses to this question differed significantly from the fellows' responses (*P* = .003) and the residents' responses (*P* = .001). Compared with faculty respondents, more fellows and residents indicated that their attendance had increased "much more" and "slightly more" as a result of the complimentary food (Table 4).

Table 3. Responses to the Question "Are you more or less likely to attend Medical Grand Rounds because of free food?"

	Respondents, %			
Response	Total* (n = 442)	Faculty†‡ (n = 261)	Fellow† (n = 74)	Resident‡ (n = 86)
Much more likely	30.3	21.8	51.4	44.2
Slightly more likely	39.8	44.1	28.4	38.4
Not at all	24.7	28.7	16.2	12.8
Less likely	2.3	1.9	2.7	3.5
Very unlikely	2.9	3.4	1.4	1.2

*Total includes respondents who were not physicians.
†Faculty vs fellows (P < .001).
‡Faculty vs residents (P < .001).

Table 4. Responses to the Question "How has your attendance at Medical Grand Rounds changed as a result of free food?"

	Respondents, %			
Response	Total* (n = 442)	Faculty†‡ (n = 262)	Fellow† (n = 73)	Resident‡ (n = 86)
Much more frequent	14.9	10.7	26.0	22.1
Slightly more frequent	38.7	35.9	42.5	47.7
Not at all	44.1	51.1	28.8	27.9
Less frequent	1.4	1.1	1.4	2.3
Much less frequent	0.9	1.1	1.4	0.0

*Total includes respondents who were not physicians.
†Faculty vs fellows (P = .003).
‡Faculty vs residents (P = .001).

In response to the question "How would your attendance at MGR change if food ceased being provided free of charge?" 53.1% of respondents indicated that their attendance would decrease, whereas 44.0% indicated that their attendance would not change. The faculty's responses to this question differed significantly from the fellows' responses (P < .001) and the residents' responses (P < .001). Compared with fellow and resident respondents, a much larger percentage of faculty respondents indicated that their attendance would not change. Compared with faculty respondents, more fellow and resident respondents indicated that their attendance would decrease (Table 5).

Table 5. Responses to the Question "How would your attendance at Medical Grand Rounds change if food ceased being provided free of charge?"

	Respondents, %			
Response	Total* (n = 441)	Faculty†‡ (n = 262)	Fellow† (n = 74)	Resident‡ (n = 86)
Increase significantly	0.5	0.8	0.0	0.0
Increase somewhat	2.5	3.5	1.4	1.2
No change	44.0	51.5	28.4	25.6
Decrease somewhat	40.6	37.3	48.6	48.8
Decrease significantly	12.5	6.9	21.6	24.4

*Total includes respondents who were not physicians.
†Faculty vs fellows (P < .001).
‡Faculty vs residents (P < .001).

When asked if food is a distraction (eg, because of noise) at MGR, most respondents (80.3%) indicated that the food was not a distraction. This response was similar among residents, fellows, and faculty. Among all respondents, 81.7% disagreed with the fol-

lowing statement: "The DOM receives unrestricted support from industry to pay for food at MGR. As a result, industry representatives have influence over MGR."

Discussion

Ours is the first systematic study assessing the effects of complimentary food on attendance at MGR. We found that, compared with attendance during the pre-complimentary food period, MGR attendance during the complimentary food period was significantly greater. These results suggest that providing free food may enhance attendance at MGR. The survey administered at the conclusion of the study period adds to these findings. A majority of respondents indicated that they were more likely to attend MGR because of the complimentary food and that their attendance increased because of it (although, compared with residents and fellow respondents, fewer faculty respondents reported that their attendance at MGR increased as a result of the complimentary food).

A number of factors (eg, program content and barriers to attendance) affect physician attendance at CME activities [13]. Survey data indicate that several barriers affect physicians' decisions to attend MGR, such as conflicting meetings, little presenter-attendee interaction, and inconvenient location [3]. Likewise, survey data indicate that some institutions provide complimentary food in an attempt to improve attendance at MGR [3]. Given that MGR occurs at noon at our institution, complimentary food not only removes a barrier (ie, by eliminating the need to choose between seeking food and attending MGR) but also adds an incentive for attending MGR (complimentary food). Some have described incentives as "the cornerstone of modern life" [14], and commonly acknowledged incentives for attending MGR, such as gaining new knowledge and CME credit, may not be sufficient for maintaining attendance. Although some view incentives negatively, incentives can be effective [5,6,8,14]. Therefore, as one examines strategies to increase attendance at MGR, one should consider not only removal of barriers but also the effect of incentives.

Although providing complimentary food may be associated with increased attendance at MGR, it also increases the cost of conducting MGR, which, for many departments, is the most expensive conference to conduct [3]. The cost of providing complimentary food at MGR at our institution is approximately $60,000 per year. To defray these costs, many departments, including ours, have garnered industry (eg, pharmaceutical) financial support [1-3,15,16].

Industry support of MGR raises the ethical concern of industry influence over MGR organizers, content, speakers, and attendees [1-3,17,18]. This concern can be addressed by using the following guidelines: 1) industry support should be unrestricted; 2) MGR speakers should disclose to attendees any conflicts of interest; 3) industry representatives should not determine MGR content; and 4) presentations at MGR should be unbiased, especially when the industry sponsor's products are discussed [3,19,20]. These guidelines are rigorously followed at our institution. Notably, our MGR attendees did not perceive inappropriate industry influence over the conference. However, measuring the influence of industry support by self-report may be biased. A recent study concluded that physicians' attitudes regarding industry support of CME activities may be biased (ie, those attending industry-supported activities are less likely to report bias than those to other educational activities. Future research should attending non-industry-supported activities) [21]. address these limitations.

Our study has several limitations. Although we used a prospective, before-and-after design, our study was neither randomized nor blinded. However, such a design would have been impractical. We could not control for or compare the quality of presentations during the 2 study periods, and, therefore, we do not know whether this factor contributed to an increased attendance at the MGR sessions. However, we compared attendance data matched for time of year to

minimize bias (eg, related to holidays). Furthermore, advertisement of MGR did not change during the 2 study periods. We did not change the time of day or the day of the week that MGR was held during the study period. In addition, although our survey data suggest that faculty, fellows, and residents may behave differently in response to complimentary food as an incentive for attending MGR, we were unable to break down the attendance data according to attendee training status. Furthermore, we were unable to break down the attendance data by physician versus nonphysician attendees. Finally, although providing complimentary food at MGR at our institution was associated with increased attendance, our results may not be generalizable to other institutions. Likewise, care should be taken when applying our results

Conclusion

Increased attendance at MGR occurred after complimentary food was provided to MGR attendees. Our data suggest that faculty, fellows, and residents are more likely to attend MGR if complimentary food is provided and less likely to attend if complimentary food is not provided. Most attendees do not perceive the complimentary food to be a distraction, nor do they perceive inappropriate industry influence over the conference. Providing complimentary food may be an effective strategy for increasing attendance at MGR.

Abbreviations

CME, continuing medical education

DOM, Department of Medicine MGR, medical grand rounds

Competing interests

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

Authors' contributions

PSM, NFL, SCL, AT, and TMH conceived of the study. CMS, PSM, and MLR carried out the literature review. CMS, PSM, NFL, SCL, AT, and TMH designed the survey evaluating attendee attitudes. CMS compiled the data and performed the statistical analyses. CMS, PSM, MLR, NFL, SCL, AT, and TMH prepared and reviewed the manuscript. All authors read and approved the final manuscript.

Appendix 1 – Survey Questions

In addition to indicating their position (ie, faculty, fellow, or resident), respondents were asked the following questions about medical grand rounds (MGR) (with accompanying choices):

1) On average, how frequently do you attend MGR? (weekly, monthly, 4 to 6 times per year, 1 to 2 times per year, never)

2) Are you more or less likely to attend MGR because of free food? (much more likely, slightly more likely, not at all, less likely, very unlikely)

3) How has your attendance at MGR changed as a result of free food? (much more frequent, slightly more frequent, not at all, less frequent, much less frequent)

4) How would your attendance at MGR change if food ceased being provided free of charge? (increase significantly, increase somewhat, no change, decrease somewhat, decrease significantly)

5) Indicate your agreement with the following statement: Food is a distraction (eg, due to noise) at MGR. (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree)

6) Indicate your agreement with the following statement: The Department of Medicine receives unrestricted support from industry to pay for food at MGR. As a result, industry representatives have influence over MGR (eg, speaker choice and content). (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree)

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This study was approved by the Mayo Clinic Institutional Review Board. Participants completed the survey anonymously and at their own discretion.

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PHARMACOENVIRONMENTOLOGY – A COMPONENT OF PHARMACOVIGILANCE

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According to WHO, Pharmacovigilance activities are done to monitor detection, assessment, understanding and prevention of any obnoxious adverse reactions to drugs at therapeutic concentration on animal and human beings. However, there is also a growing focus among scientists and environmentalists about the impact of drugs on environment and surroundings. The existing term 'Ecopharmacology' is too broad and not even defined in a clear manner. The term 'Pharmacoenvironmentology' seeks to deal with the environmental impact of drugs given to humans and animals at therapeutic doses.

Background

With growing technological advances, newer and more effective drugs are being manufactured and are used on an ever-growing scale for people with various medical conditions. Pharmacovigilance activities are done to monitor any obnoxious reactions of these drugs at therapeutic concentrations. With growing research in the field of ecology and environment, many of the adverse effects of these drugs on the environment have come to light. The first study that detected drugs in sewage took place in 1976 at the Big Blue River sewage treatment plant in Kansas City [1]. In the meantime, a number of findings related to rising levels of some drugs and their adverse effects on the flora and fauna has necessitated some action by regulatory agencies like the FDA and the European Union. Still, there lacks a substantial protocol for prospective monitoring of drug concentrations in the environment and the evident adverse effects.

Discussion

We are living in an environment that is polluted not only by heavy metals, pesticides, and emissions from gasoline engines, but also with pharmaceutical chemicals. These pharmaceuticals enter into the environment through various routes causing harmful effects.

Literature on the above subject was searched in almost all major search engines including PubMed with the keywords – Ecopharmacology, Pharmaceuticals and Personal Care Products (PPCPs), Clinical trials and Environment. A number of studies measuring the levels in surface water, groundwater and drinking water of some drugs given therapeutically to humans and animals including antibiotics, hormones, pain killers, tranquilizers, beta blockers and anticancers were found [2-8]. Development of antibiotic resistance in pathogens in the environment owing to their exposure was the major concern. Richard and Cook even proposed a mechanistic approach to the exposure analysis for environmental risk assessment [9]. Some prominent examples of drugs causing harmful effects on environment are that of vultures' death after consuming carcasses of animals treated with Diclofenac sodium [10-12], Ethi-nyl estradiol adversely affecting fish through its "femini-zation" of males [13], antidepressant drugs like.

Fluoxetine (Prozac) triggering spawning in shellfish and traces of Cocaine detected in River Thames [14]. A few drugs are so synthesized that they tend to persist in the environment even after their excretion. Clofibric acid in the aquatic environment disturbing the local fauna is an example.

When a human or animal is given a drug orally, it may either be fully or poorly absorbed from the gastrointestinal tract. Clearly, unabsorbed drug will pass into the environment along with faeces. When humans or animals are given drugs parenterally or orally, the drug may be metabolized to a greater or lesser extent and excreted into the environment (including in exhaled air) as parent drug or metabolites, or as a mixture of

both. It means that once they are excreted into the environment, they enter food chains and concentrate as they move upward into larger predators [15]. Ecopharmacology (Ecosystem + pharmacology) describes entry of chemicals or drugs into the environment through any route and at any concentration disturbing the balance of ecology (ecosystem), as a consequence. If these drugs enter through living organisms via elimination subsequent to pharmacotherapy, it should be a specific domain of pharmacology and not of environmental studies. This domain may be referred as Pharma-coenvironmentology. Apart from that, Ecopharmacology as a major term should be restricted to studies of "PPCPs" irrespective of doses and route of entry into environment. PPCPs comprise a very broad and diverse collection of groups of chemicals substances comprising all human and veterinary drugs (available by prescription or over-the-counter; including the new genre of "biologics"), diagnostic agents, "nutraceuticals" (bioactive food supplements), and other consumer chemicals, such as fragrances, cosmetics and sun-screen agents, "excipients" (so-called "inert" ingredients), biopharmaceuticals, dyes, pesticides, and many others [16]. This broad collection of substances refers, in general, to any product consumed by individuals for personal health or cosmetic reasons. The term Pharmacoenvironmentology can be used for this specialty dealing specifically with pharmacological agents and their impact on the environment, after elimination from humans and animals as post-therapy.

Though a number of regulatory bodies like the FDA and the European Union have set some cut-off limit for environmental concentration of drugs, no actual testing is conducted after a drug is marketed to see if the environmental concentration was estimated correctly.

When a new drug is proposed for market, FDA requires the manufacturer to conduct a risk assessment that estimates the concentrations that will be found in the environment. If the risk assessment concludes that the concentration will be less than one part per billion, the drug is assumed to pose acceptable risks. FDA has never turned down a proposed new drug based on estimated environmental concentrations, and no actual testing is conducted after a drug is marketed to see if the environmental concentration was estimated correctly [17]. Apart from that there is little concern and research to find the adverse effects on environment, of particular drugs given at therapeutic doses. Even in clinical trials, where many limitations like that of limited size, narrow population, narrow indications and short duration are observed, we also found that evaluation of drugs on environment is practiced very minimally.

The European Union has described a two-phased approach to evaluate Medicinal Products in environment. The environmental concentration of the medicinal product is calculated in Phase I. Substances with a very high specific mode of action like hormones are directed to Phase II irrespectively of the result of the exposure calculation. In the second phase, information on the physical, chemical and toxicological properties are obtained and assessed in relation to the environmental exposure of the medicinal product [18]. Similarly, environmental risk assessments are also an integral part of the assessment process in the granting of marketing authorizations for veterinary medicinal products [19]. According to John P. Sumpter (2007), these recent European Medicines Agency guidelines covering the environmental risk assessment of human pharmaceuticals are a step in the right direction, but a more sophisticated approach, rather than a "one-fits-all" solution, is probably needed [20]. As a part of a Good Clinical Trial, studies on impact of particular drugs on the environment should too be incorporated. Some concerns that need to be taken up under Pharma-coenvi-ronmentology are that of drugs and their exact concentration in different components of the environment.

Conclusion

Pharmacovigilance pertains to the activities of adverse effects of drugs at therapeutic doses on animal and human beings. In this context, Pharmacoenvironmentology may be an extension of Pharmacovigilance dealing specifically with the effects pertaining to the environment and ecology of drugs given in therapeutic concentrations. Pharmacologists having this particular expertise (pharmacoenvironmentologist) may be made a compulsory component of the team assessing different aspects of drug safety. We need to monitor the effects of drugs not only as a good medical practice, but also to safeguard our environment.

Competing interests

Authors do not have any conflict of interest with any organization both personally and financially. Thus, the authors declare that they have no competing interests.

Authors' contributions

All authors have made substantial contributions while writing this paper right from conception and design, acquisition of data and finally in the analysis and interpretation of the data. All authors have also been involved in drafting the manuscript and revising it critically for important intellectual content. We give final approval of the version to be published. Each author has participated sufficiently in the work to take public responsibility for appropriate portions of the content. All authors have read and approved the final manuscript.

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DAILY RHYTHM OF SALIVARY AND SERUM UREA CONCENTRATION IN SHEEP

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In domestic animals many biochemical and physiological processes exhibit daily rhythmicity. The aim of the present study was to investigate the rhythmic pattern of salivary and serum urea concentrations in sheep.
Six 3-year-old female sheep kept in the same environmental conditions were used. Sheep were sampled at 4 hour intervals for 48 consecutive hours starting at 08:00 of the first day and finishing at 04:00 of the second day. Blood samples were collected via intravenous cannulae inserted into the jugular vein; saliva samples were collected through a specific tube, the "Salivette". Salivary and serum urea concentrations were assayed by means of UV spectrophotometer. ANOVA was used to determine significant differences. The single Cosinor procedure was applied to the results showing significant differences over time.
ANOVA showed a significant effect of time on salivary and serum urea concentrations. Serum and salivary urea peaked during the light phase. In the dark phase serum and salivary urea concentrations decreased, and the diurnal trough occurred at midnight. Cosinor analysis showed diurnal acrophases for salivary and serum urea concentrations. Daily mean levels were significantly higher in the serum than in the saliva.
In sheep both salivary and serum urea concentrations showed daily fluctuations. Urea is synthesized in the liver and its production is strongly influenced by food intake. Future investigation should clarify whether daily urea rhythms in sheep are endogenous or are simply the result of the temporal administration of food.

Background

The circadian clock, an endogenous timing system, generates biochemical, physiological and behavioural rhythms. To be useful, these clocks must be synchronized (*entrained*) to environmental time cues (*zeitgebers*). The primary environmental zeitgeber is light, and the regular daily change in light intensity at dawn or dusk seems to determine the circadian photo entrainment. Circadian rhythms have been described in many animal species, including livestock [1,2]. Some molecular studies on rodents identified the liver as the site of a putative foodentrainable oscillator [3], which could be synchronized by feeding time [4,5]. Few studies were carried out on the rhythmicity of liver function in farm animals. Serum concentration of urea was evaluated in cows during different feeding schedules [6] and in goats maintained under various schedules of lighting and feeding [7] in order to understand the mechanisms of entrainment of liver function. Ruminants, such as sheep and cattle, secrete a large amount of saliva from the salivary glands into the rumen (≥100 litre/day in cattle and ≥10 litre/day in sheep). In ruminants, the recycling of urea to the fore stomach is an importance source of nitrogen for synthesis of microbial protein [8,9]. For a given diet, the amount of urea recycled to the rumen, both in saliva and across the rumen wall, is directly related to the amount of urea synthesized which, in turn, is related to nitrogen intake and the degradability of dietary nitrogen. This explains how serum urea concentration is strictly related to feeding: when a nitrogen-deficient ration is ingested, urea does not pass into the urine but is converted into microbial protein in the digestive tract, to be re-utilized [10]. Both salivary secretion and direct diffusion through the rumen wall are responsible for the appearance of serum urea in the digestive tract. In sheep, a high correlation between urea concentration in parotid saliva and in plasma was also observed [11]. The defining of the liver as a site of a putative food-entrainable oscillator and the existence of a daily rhythm of serum urea concentration influenced by feeding in rumi-

nants led us to investigate the rhythmic pattern of both salivary and serum urea concentrations in sheep.

Methods

Six 3-years-old female sheep (*Ovis aries*, Comisana breed; mean body weight 48.0 ± 2.0 kg) clinically healthy, non-pregnant and non-lactating, were used. Animals were housed in individual boxes and kept under natural photo-thermoperiodic conditions (longitude: 15° 33' 24" E, latitude: 38° 12' 27" N; sunrise: 05:52, sunset: 17:43). Starting 30 days before the test, all sheep were fed with hay *ad libitum* and concentrate 250 g/day (oats 25%, corn 34%, mineral vitamin supplement 3% and barley 38%) once each day at 07:00 h. Water was available *ad libitum*. After this preconditioning period, saliva and serum samples were collected every 4 hours for two consecutive days (starting at 08:00). Protocols of animal husbandry and experimentation followed applicable regulations in Italy. Salivary samples were collected through a specific tube, the "Salivette®"(SARSTEDT, Germany), which provides a standardized method for the easy and safe collection of saliva. Briefly, the "salivette" is a tube containing a swab used to absorb the saliva. The swab was attached to a nylon thread and inserted in the mouth. Sheep were stimulated to chew for 1–2 minutes to fill the swab with as much saliva as possible. To recover a saliva sample (0.5–1.5 ml) from the swab, the salivette was centrifuged at 2000 Ч g for 2 minutes. The swab was removed from the salivette and the saliva collected in the tube for analysis. Saliva obtained was immediately stored at -20°C until assayed. Blood samples (5 ml) were collected using jugular intravenous catheters (FEP 20 g 1 Ч 32 mm; Delta Med, Italy) into tubes *Vacuitainer* without anticoagulant. Blood samples clotted at room temperature for 1 h and were subsequently centrifuged at 3000 Ч g for 20 min (4235 A, ALC, Italy). The obtained sera were stored at -20°C until assayed. Salivary and serum urea was analyzed with a standard kit (SEAC, Italy) by means of a UV spectropho-tometer (SEAC, Italy). The urea kit is based on the breakdown of urea into ammonia and CO_2 by the action of urease followed by the synthesis of glutamate and NAD+ by the reaction of ammonia, α-chetoglutarate and nicoti-namide adenindinucleotide. All the results were expressed as mean ± SD. Data were normally distributed ($p < 0.05$, Kolmogorov-Smirnov test) and one-way or two-way repeated measures analysis of variance (ANOVA) was used to determine significant differences (p values < 0.05 were considered statistically significant). Bonferroni's Multiple Comparison test was applied for post hoc comparison. To compare overall levels of urea in the different analyses, mean urea levels over a daily period were used. Data were analyzed using the software STATISTICA 5.5 (StatSoft Inc., USA). In addition, we applied a trigonometric statistical model to the average values of each time series, so as to describe the periodic phenomenon analytically, by individuating the main rhythmic parameters according to the single cosinor procedure [12]: Mesor (Midline Estimating Statistic of Rhythm), expressed in the same conventional unit of the relative parameter, with the confidence interval (C.I.) at 95%, Amplitude (A), expressed in the same unit as the relative Mesor, and Acro-phase (Φ), expressed in hours with 95% confidence intervals.

Results and Discussion

ANOVA showed a robust daily rhythm of urea in serum and saliva of sheep (serum: $F_{(11,55)} = 69.64$, $p < 0.0001$; saliva: $F_{(11,55)} = 30.25$, $p < 0.0001$; one-way ANOVA). Both urea profiles showed high levels during light phases and low during dark phases (Figure 1). The application of the periodic model and a statistical analysis of the cosinor enabled us to define the periodic parameters and their acrophases (expressed in hours) during the 2 days of monitoring. Table 1 shows the MESOR, with the fiducial limits at 95%; the amplitude, expressed in the same unit as the relative MESOR; the acrophase, calculated using the single cosinor method and expressed in hours, together with the confidence interval at 95%, for the periodic serum and sali-

vary urea concentrations. Serum and salivary urea showed similar diurnal acrophases: serum urea at 12.24 (day 1) and at 11.56 (day 2), salivary urea at 12:00 (day 1) and at 12:12 (day 2).

Serum urea values were significantly different from salivary values ($F(1,66) = 464.8$, $p < 0.0001$; two-way ANOVA). Particularly, daily mean levels were significantly higher in the serum (5.17 ± 0.15 mmol/l; mean ± SEM) than in the saliva (2.9 ± 0.09 mmol/l).

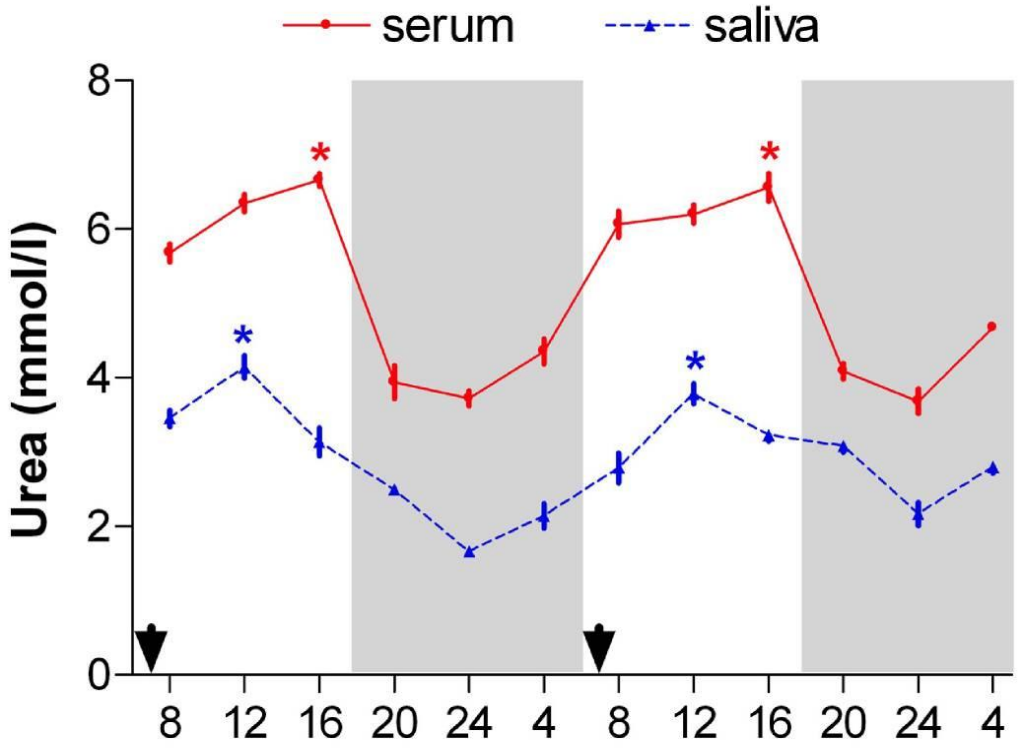

Figure 1. Daily rhythms of serum and salivary urea concentrations in sheep.

Both urea profiles showed clear diurnal rhythms: urea levels were high during the light phase and low during the dark phase of the natural light-dark cycle. Each point represents mean ± SEM. Gray bars indicate the dark phase of the natural light-dark cycle. Arrowheads indicate times of feeding. Asterisks indicate peaks of urea concentrations.

Our results are comparable to those of a previous study on sheep fed twice a day, in which serum urea levels showed diurnal acrophases at 16:00 [13]. The small difference in acrophases may be explained by differences in the feeding regimes. In fact, investigations in small ruminants have shown that serum urea concentration exhibited daily fluctuations only in the presence of a daily feeding regime: a robust daily rhythm was observed in goats fed once each day, which vanished when animals were food deprived [7].

Our results cannot exclude the possibility that the increase of urea from 04:00 to 08:00 was due to the start of feeding at 07:00. Other investigations clearly showed a circadian rhythm of urea with diurnal peaks in cows [14] and documented the effect of different feeding schedules on daily rhythms of serum urea and ammonia concentration [6,15]. Monogastric animals also showed a daily rhythm of plasma urea concentration with diurnal acrophases [13]. For instance, peaks of plasma urea concentration were reached 4 hours after feeding in pigs fed twice each day compared to subjects fed *ad libitum* [16].

Table 1. Mesor (M), fiducial limits (F.L.) at 95%, Amplitude (A) and Acrophase (Φ), expressed in hours, with confidence interval (C.I.) at 95%, of serum and salivary urea during the two days of study

	MESOR	F.L. 95%	A	Φ	C. I. 95%
Serum urea					
Day 1	5.12	(4.56–5.67)	1.56	12:24	(08:16–16:32)
Day 2	5.21	(4.66–5.76)	1.48	11:56	(07:36–16:16)
Salivary urea					
Day 1	2.84	(2.59–3.09)	1.16	12:00	(09:44–14:16)
Day 2	2.75	(2.49–3.01)	0.72	12:12	(08:04–16:20)

Conclusion

Here we showed a non-invasive method to measure daily variations of urea concentrations. However, we must consider that urea levels in the saliva are significantly lower than in the serum. Serum and salivary urea are synthesized in the liver and their production is strongly influenced by food intake. Our results suggest the influence of external stimuli (feeding time) on the rhythmic pattern of metabolites involved in liver function, possibly acting on circadian clocks in the liver and the suprachiasmatic nucleus, which could be very important for the ability of organisms to synchronize their internal physiology. Future investigation should clarify whether daily urea rhythms in sheep are endogenous or are simply the result of the temporal administration of food.

Competing interests

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

Authors' contributions

GP directed the study, participated in data collection and wrote the final version of the manuscript. AF participated in the design of the study. CB participated in the design of the study and performed statistical analysis. GC participated in the design of the study and helped with its coordination. All authors read and approved the final version of the article.

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THE EFFECT OF HIGH CORRELATED COLOUR TEMPERATURE OFFICE LIGHTING ON EMPLOYEE WELLBEING AND WORK PERFORMANCE

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The effects of lighting on the human circadian system are well-established. The recent discovery of 'non-visual' retinal receptors has confirmed an anatomical basis for the non-image forming, biological effects of light and has stimulated interest in the use of light to enhance wellbeing in the corporate setting.
A prospective controlled intervention study was conducted within a shift-working call centre to investigate the effect of newly developed fluorescent light sources with a high correlated colour temperature (17000 K) upon the wellbeing, functioning and work performance of employees. Five items of the SF-36 questionnaire and a modification of the Columbia Jet Lag scale, were used to evaluate employees on two different floors of the call centre between February and May 2005. Questionnaire completion occurred at baseline and after a three month intervention period, during which time one floor was exposed to new high correlated colour temperature lighting and the other remained exposed to usual office lighting. Two sided t-tests with Bonferroni correction for type I errors were used to compare the characteristics of the two groups at baseline and to evaluate changes in the intervention and control groups over the period of the study.
Individuals in the intervention arm of the study showed a significant improvement in self-reported ability to concentrate at study end as compared to those within the control arm ($p < 0.05$). The mean individual score on a 5 point Likert scale improved by 36.8% in the intervention group, compared with only 1.7% in the control group. The majority of this improvement occurred within the first 7 weeks of the 14 week study. Substantial within group improvements were observed in the intervention group in the areas of fatigue (26.9%), alertness (28.2%), daytime sleepiness (31%) and work performance (19.4%), as assessed by the modified Columbia Scale, and in the areas of vitality (28.4%) and mental health (13.9%), as assessed by the SF-36 over the study period.
High correlated colour temperature fluorescent lights could provide a useful intervention to improve wellbeing and productivity in the corporate setting, although further work is necessary in quantifying the magnitude of likely benefits.

Background

Until now the main purpose of indoor lighting has been to aid visually directed tasks in the absence of sufficient external light. There is, however, increasing evidence to suggest that the brightness and wavelength of ambient light is not only important for task completion, but that it can also have strong non-visual biological effects, regulating the human circadian system, and impacting upon the biological clock, mood and alertness.

A number of studies have provided support for the beneficial effects of light, demonstrating a positive influence on vitality, depressive symptoms [1], alertness. [2], psy-chomotor vigilance and task performance. [3], morning cortisol levels [4], and even sleep quality [5,6]. Additionally, bright-light exposure during winter appears to be effective at improving health-related quality of life and alleviating distress [7]. Exposure to bright light in the morning and evening in the workplace has also been shown to improve self-reported mood, energy, alertness and productivity in individuals with "sub-syndromal seasonal affective disorder" [8].

The recent discovery of 'non-visual' retinal receptors has confirmed an anatomical basis for the observed biological effects of light, with the photopigment melanopsin playing an essential role in phototransduction [9]. As such, light has a broad regulatory impact on human physiology within virtually all tissues in the body with action spectra in humans showing the peak sensitivity for these

effects to be in the short wavelength portion of the spectrum. [10,11].

It has been suggested that the relative shortage of daylight exposure for office workers during daily life may compromise their health and wellbeing, which in turn has stimulated interest in the applications of light in the corporate setting. Of particular relevance is the fact that whilst outdoor illuminance typically ranges between 2000 and 100,000 lux, indoor office illuminance is usually considerably lower, with norms of approximately 500 lux. Moreover, typical fluorescent indoor lighting contains considerably less short wavelength "blue spectrum" light than natural daylight, precisely the component of the spectrum thought to be highly relevant for achieving non-visual, biological effects.

The amount of blue light in the spectrum of light sources increases with increasing colour temperature. So far a number of studies have investigated the effects of the colour temperature of lighting on mental activity, the central nervous system and alertness. These studies have demonstrated that higher colour temperatures (7500 K versus 3000 K) are more activating from the viewpoint of mental activity level [12]. Both the parasympathetic and sympa-thetic nervous systems are thought to be enhanced under higher colour temperature conditions. [13] and drowsiness has been observed to be higher under lower colour temperature lighting when comparing 3000 K with 5000 K [14].

Whilst findings of previous studies have been encouraging, these have been based on very small sample sizes and generally conducted within carefully controlled laboratory type environments. There is currently little understanding of the effect of lighting conditions outside such a setting, such as in the workplace. The current study addresses this issue, at least in part, with its relatively large sample size and the fact that it was conducted in a 'real world' workplace setting.

Understanding of the action spectra of many non-visual, biological effects remains far from comprehensive. Nocturnal melatonin suppression is probably the most frequently studied non-visual, biological effect of light. Its action spectrum is well established and appears to be most sensitive to short wavelength light. [10,11]. Also, in achieving phase advancing [15] or alerting effects. [16,17], short wavelength light is reported to be more effective as compared to longer wavelength light. It is therefore reasonable to assume that a first estimate of the non-visual effects of a light source can be derived from the action spectrum for nocturnal melatonin suppression. Using this assumption,17000 K lamps would be expected to be 1.55 times as effective as compared to daylight at equal illuminance in achieving non-visual biological effects, and in comparison to standard low colour temperature lighting of 3000 K could be expected to be 2.4 times as effective. With this background information in mind, it can be postulated that the new high correlated colour temperature lights would have significant effects upon feelings of wellbeing, alertness, concentration and possibly work performance in those exposed to it.

The aim of this study was to quantify the effects of newly developed high correlated colour temperature fluorescent lighting on functioning, well-being and work performance of individuals working within a call-centre.

Methods

A prospective, controlled intervention was conducted involving study participants working as call-handlers on two floors of the offices of Standard Life Healthcare (SLH) in Stockport, UK. SLH is a shift-working call centre with long working days spanning 8 am–8 pm, divided into early and late shifts. The two floors used for the study are identical in their layout and operational function within the organisation. Each floor is equipped with 600 mm square recessed luminaries with aluminium louver (4 Ч 6 cells) and four 18 W fluorescent tubes. The lumi-

naire spacing is 2.4 m Ч 2.4 m. Each work area has dark floors and white walls. Floors have windows on approximately 80% of both their East and West wall areas. Blinds are present and used in such a way that typically more than 50% of the window area is covered.

At baseline both floors were illuminated with lights with a correlated colour temperature of 2900 K. Throughout the study, the lighting on one floor (floor B) was unchanged, with employees working on this floor being used as the control group. On the other floor (floor A), a lighting intervention was implemented after baseline measurements. The intervention involved a lamp change to the entire lighting system on this floor, with all existing fluorescent lamps being replaced by new high correlated colour temperature fluorescent lamps (ActiViva Active, Philips). These lamps contain an enhanced amount of short wavelength light with a resulting higher colour temperature of 17000 K. Figure 1 shows the spectral power distribution of the new lamps. The lamp change occurred on a non working day (Sunday) and participants were not informed of whether theirs was the intervention or control arm of the study.

Before the lamp change, horizontal and vertical illlumi-nance values were determined on more than 10 desks from each floor, deemed representative of the range of working conditions. The horizontal illuminance was measured at the working plane (desk surface). The vertical illuminance was measured at the eye position, when sitting behind the desk. After the lamp change the illuminance values at each desk were measured once with artificial lighting switched on, and once with it switched off. This allowed estimation of the daylight contribution to the indoor illuminance. All measurements were taken at noon on a cloudy winter day.

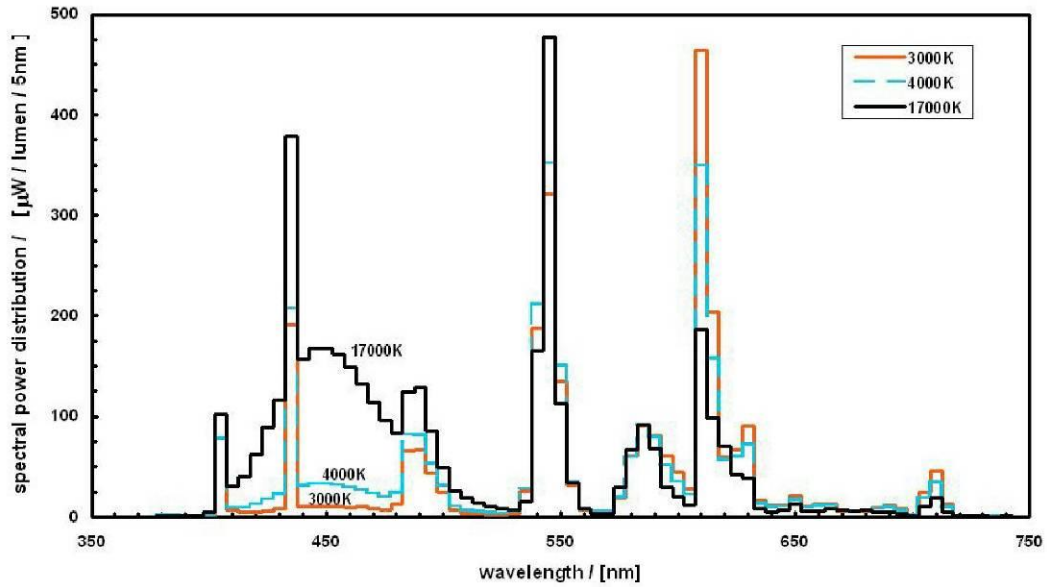

Figure 1. Spectral power distribution of the high (17000 K) correlated colour temperature lamps. The spectral power distributions of typical 3000 K and 4000 K fluorescent lamps are plotted for comparison.

Participation in the study was voluntary; those who did not wish to participate were offered seating in a different part of the building. Individuals were informed that the aim of the study was to assess the acceptability of a new type of indoor lighting. They were informed that the lighting would be changed on both floors and that they would be required to complete online questionnaires during the 14 weeks of the study. Participants were not informed that the aim of the study was to assess any particular aspect of work

performance or wellbeing and were not told which floor would receive the new lighting technology. All participants digitally accepted the terms and conditions and provided their consent to participate in the study prior to completing the questionnaires.

The lights used in the study have passed all appropriate European Union safety standards and are in general production. We were informed by the Central Office for Research Ethics Committees in the UK that ethical committee approval was not required for this study.

Data collection

Individuals' alertness, performance, concentration and health related quality of life were assessed by means of two online questionnaires. The questionnaires were completed on three separate occasions, at baseline (week 1, 7– 11th February 2005), week 7 and week 14. Questionnaires completion took approximately 20 minutes and was done at one sitting during the working day.

The first questionnaire was a modification of the Columbia Jet Lag Scale [18], originally designed to quantify changes in alertness, memory, fatigue and general wellbe-ing associated with crossing time zones. Although the current study was not assessing jet lag, the majority of the constructs quantified by the questionnaire was relevant to the shift-working practices of the call centre. Nine of the eleven items of the questionnaire were derived directly from the original instrument with possible answers of (i) not at all, (ii) a little bit, (iii) moderately, (iv) quite a bit and (v) extremely. Scores were attributed to each item from 1 to 5 depending upon the response (1 = not at all to 5 = extremely) for a combined overall score out of 45. A high score indicated significant issues with alertness, lethargy, sleepiness and concentration and a low score indicated few or no issues. The nine items were:

Over the last 3 days how much have you been bothered by:

1. Fatigue or tiring easily
2. Trouble concentrating or thinking clearly
3. Physical clumsiness
4. Decreased daytime alertness
5. Trouble with memory
6. General feelings of weakness
7. Light headed, dizzy, or other uncomfortable sensations in the head
8. Lethargy and sluggish feelings
9. Sleepiness during the day

The other two items were (i) self assessed job performance, which was derived from the World Health Organisation Health and Work Performance Questionnaire (WHO-HPQ) and (ii) self assessed overall alertness and concentration:

10. On a scale of 1 to 10, where 1 is the worst performance anyone could have at your job and 10 is the performance of a top worker, how would you rate your overall performance over the last 3 days?
11. On a scale of 1 to 10, where 1 is not alert at all and 10 is fully alert. All things considered, how alert and able to concentrate have you been over the last 3 days?

The second questionnaire was the short form 36 (SF-36) health related quality of life instrument with standard scoring performed according to the published literature [19]. Only certain items from this questionnaire were of particular interest to this study; however, the questionnaire was administered in its entirety in order to avoid introducing bias in responses given to this previously well validated instrument [20]. On final questionnaire completion, at the end of the study, participants on both floors were asked to comment about the lighting on their floor. Specifically, they were asked whether it was liked or disliked and whether they wished to keep the current lighting or revert to previous lighting conditions.

Data analysis

Digitally collected data were transferred to STATA version 8.2 for analysis. All datasets were checked for outliers and errors to ensure that all responses fell within the expected range of values prescribed by the two questionnaires. Coding of SF-36 items and derived measures was conducted according to validated literature guidelines. [21].

A combined measure was derived by summing the initial 9 items in the modified Columbia jet lag scale yielding a maximum possible score of 45 and a minimum of 9. All data collection and storage was compliant with the UK Data Protection Act 1998.

Table 1. Horizontal and vertical desk illuminance values on the intervention and control floors.

Floor	Average horizontal illuminance at working plane (SD)	Average % daylight contribution to horizontal illuminance (SD)	Average vertical illuminance at the eye position (SD)	Average % daylight contribution to vertical illuminance (SD)
A. Intervention (17000 K)	311 lux (112)	13% (10)	170 lux (85)	40% (33)
B. Control (2900 K)	354 lux (45)	11% (10)	128 lux (44)	55% (32)

All items from the modified Columbia Jet Lag Scale were utilised in the analysis as these were all measures relevant to the principle aims of the study, i.e. workplace functioning, wellbeing and work performance. Five of the SF-36 combined measures were utilised in the analysis (General Health, Vitality, Social Functioning, Role Emotional and Mental Health), as again these were the constructs considered relevant to the main study aims.

The distribution of variables by floor and the mean score for each item was obtained for the range of measures described above. The selected SF-36 combined measures were compared with US norms. [21] in order to assess the generalisability of findings.

Two-sided unpaired t-tests were used to compare baseline characteristics between the control and intervention floors. Significance was obtained on 67 degrees of freedom (d.f.). The within-floor improvements over the study period were ascertained by examination of percentage mean improvement by group compared to baseline scores, and by using two-sided paired t-tests on 22 and 45 d.f. respectively. Finally, two-sided unpaired t-tests were used to examine whether there was a statistically significant difference in individual scores at the end of the intervention period in the two groups, controlling for individual baseline scores. A total of thirty questionnaire items or scores were examined from the two questionnaires, and a Bonferroni correction for Type I errors was accordingly applied to each set of tests based on this total number when interpreting the significance of the t-statis-tics obtained: the threshold t-statistic used to determine significance was deemed equal to probability divided by 30, the total number of questionnaire items examined.

Results

Sixty-nine individuals agreed to take part in the study (23 on the control floor and 46 on the intervention floor), representing 49% of the total eligible population during the study period. There were no significant differences in the distribution of participants by gender or age by floor ($X^2 = 0.30$, $p = 0.58$; $X^2 = 0.04$, $p = 0.84$ respectively).

No statistically significant differences were observed between horizontal or vertical desk illuminance between the two floors at baseline. Differences between mean horizontal and vertical illuminance between the two floors after the lamp change were similarly non-significant (Table 1). The estimated daylight contribution to the illuminance is also documented in Table 1. The average daylight contribution to the horizontal illuminance is small (average 12%), but studied daylight contributed between 40% and 55% to the vertical illuminance.

Analysis of the distribution of variables and between group t-tests at baseline showed no significant difference in composite scores or responses to individual items

between the two floors. Tables 2 and 3 show the mean scores derived from the modified Columbia Scale and the SF-36 questionnaire at baseline and study end for both the intervention and control groups. In addition the results of between and within group t-tests are also documented.

The mean baseline SF-36 derived scales were compared to published reference

scores from a normal US population sample. [21]. Of the five SF-36 scales utilised in the study, the mean scores obtained from our study population were significantly different in three instances: the study population reported worse health status in (i) vitality, (ii) social functioning and (iii) mental health compared to the reference US population (respective two-sided t-tests and p-values after application of Bonferroni correction: -5.60 and $p < 0.001$; -4.34 and $p < 0.001$; -4.92 and $p < 0.001$). The remaining selected SF-36 scales (role emotional and general health) were not significantly different.

Table 2. Distribution of Modified Columbia Scale scores examined by group and time period.

		Baseline		Study End (3 months)		% change		Unpaired t test (df = 67)	Paired t test (df = 22)	Paired t test (df = 45)	Unpaired t test (df = 67)
Item No.	Description	Control (n = 23)	Intervention (n = 46)	Control (n = 23)	Intervention (n = 46)	Control	Intervention	Baseline comparison	Control change	Intervention change	3 month comparison
		mean (SD)	mean (SD)	mean (SD)	mean (SD)			t statistic	t statistic	t statistic	t statistic
1	Fatigue/tiring easily?	2.9 (0.9)	2.9 (1.1)	2.7 (1.1)	2.1 (1.0)	7.6	26.9	-0.16	0.93	**4.04****	1.76
2	Trouble concentrating	2.5 (1.1)	2.9 (1.2)	2.5 (0.9)	1.8 (0.9)	1.7	36.8	-1.23	0.21	**5.84****	**3.46***
3	Physical clumsiness?	2.0 (1.1)	1.7 (1.0)	1.6 (0.6)	1.5 (0.9)	21.7	13.7	1.02	1.93	1.48	-0.70
4	Decreased daytime alertness?	2.7 (1.1)	2.5 (1.2)	2.1 (0.8)	1.8 (0.8)	21.0	28.1	0.74	2.73	**3.96****	0.45
5	Trouble with memory?	2.4 (1.3)	1.9 (1.1)	2.1 (0.8)	1.5 (0.7)	12.5	21.3	1.65	1.07	2.80	0.38
6	General feelings of weakness	2.0 (1.1)	2.0 (1.0)	1.7 (0.7)	1.4 (0.8)	17.0	26.7	0.33	1.56	**3.60***	0.67
7	Light-headed & dizzy	2.2 (1.4)	2.1 (1.3)	2.0 (1.1)	1.4 (0.8)	9.8	33.7	0.26	1.10	**4.04****	1.74
8	Lethargy/sluggish feelings?	3.0 (1.0)	2.7 (1.3)	2.3 (0.8)	1.8 (0.8)	23.5	31.7	0.93	**3.43***	**5.07****	0.55
9	Sleepiness in day	3.0 (1.2)	2.8 (1.2)	2.6 (1.0)	1.9 (0.7)	14.5	31.0	0.66	2.47	**4.90****	1.55
10	Work performance	7.0 (1.7)	6.4 (1.5)	7.3 (1.6)	7.6 (1.4)	4.4	19.4	1.45	-1.16	**-6.07****	-2.72
11	Alertness and concentration	6.2 (1.8)	6.1 (1.9)	6.8 (1.7)	7.5 (1.8)	9.9	22.9	0.23	-2.13	**-4.34****	-1.57
	Combined Score (first 9 items)	22.7 (7.5)	21.5 (8.3)	19.5 (5.2)	15.4 (5.7)	14.3	28.6	0.59	2.60	**5.22****	1.53

* = $p < 0.05$, ** = $p < 0.001$ equivalent after applying Bonferroni correction

Following the three month intervention period, exploration of within-group improvements in the intervention group showed substantial and significant improvements in a number of areas. In contrast, significant differences over time were found for a smaller range of variables within the control group, with the magnitude of observed differences tending to be less. Of interest were those variables for which a statistically detectable improvement was observed in the intervention group, but not in the control group. In general those individuals exposed to the new lighting technology showed a consistent improvement in the areas of fatigue, concentration, memory, mood and energy as compared with individuals who did not have a lighting change (see Table 4). Improvements of 30% or more compared to baseline measures were observed in the areas of (i) concentration, (ii) light headedness, (iii) lethargy and (iv) sleepiness in the intervention group. In addition, the intervention population showed significant improvements in two of the five investigated SF-36 scales at study end (vitality and mental health) compared to baseline scores, which for vitality was highly significant ($p < 0.001$). In contrast, the control group only showed borderline significant improvement on the social functioning scale (Table 4).

Table 3. Distribution of selected SF-36 combined measures by group and time period.

		Baseline		Study End (3 months)		% change		Unpaired ttest (df = 67)	Paired ttest (df = 22)	Paired ttest (df = 45)	Unpaired ttest (df = 67)
Item No.	Description	Control (n = 23)	Intervention (n = 46)	Control (n = 23)	Intervention (n = 46)	Control	Intervention	Baseline comparison	Control change	Intervention change	3 month comparison
		mean (SD)	mean (SD)	mean (SD)	mean (SD)			t statistic	t statistic	t statistic	t statistic
GH	General Health	65.5 (22.4)	67.8 (20.5)	70.3 (22.0)	73.8 (17.0)	7.4	8.7	-0.44	-1.57	-2.33	-0.25
V	Vitality	43.2 (23.5)	48.4 (20.4)	50.5 (19.0)	62.1 (17.1)	17.0	28.4	-0.94	-1.95	**-4.44****	-1.25
SF	Social Functioning	63.6 (27.7)	75.0 (25.4)	81.0 (19.5)	85.6 (17.7)	27.4	14.1	-1.71	**-3.35***	-3.09	1.11
RE	Role Emotional	77.5 (29.1)	80.8 (23.8)	80.4 (27.9)	86.1 (19.5)	3.7	6.5	-0.50	-0.56	-1.53	-0.39
MH	Mental Health	62.8 (22.2)	64.3 (20.5)	67.8 (16.8)	73.3 (15.8)	8.0	13.9	-0.28	-1.78	**-3.42***	-0.93

* = $p < 0.05$, ** = $p < 0.001$ equivalent after applying Bonferroni correction

Between group comparisons at study end, controlling for baseline differences, showed the intervention group had significantly better status in the area of concentration (item 2 of the Columbia Scale) ($p < 0.01$ after Bonferroni correction for Type I errors). The chronology of the observed improvements in concentration was investigated further by additionally analysing the seven week data for this item at an individual level, in order to ascertain how rapidly the observed improvements had occurred. Table 5 shows the mean data by group at each time period with Figure 2 showing the mean individual percentage change for this item at week 7 and week 14 as compared to baseline. The observed change in the control group was in a negative direction (shown on the graph as an increase in score), with little difference between scores at week 7 or week 14. Conversely, the reduction in scores in the intervention group reflected an improvement in this measure, much of which had already occurred by week 7. The changes in the two groups is reflected by two-sided unpaired t-tests that explore the difference between the groups at each time period and are significant both at week 7 and week 14. ($t = 2.48$, $p = 0.02$ at week 7; $t = 3.46$, $p = 0.001$ at week 14).

Table 4. Areas of substantial improvement in the intervention group compared to baseline measures (where a concomitant improvement was not observed in the control group).

Area	Description	Percentage Improvement over baseline measure
Fatigue	Item of original Columbia Scale	26.9%
Concentration	Item of original Columbia Scale	36.8%
Daytime Alertness	Item of original Columbia Scale	28.1%
Feelings of Weakness	Item of original Columbia Scale	26.7%
Light-headedness	Item of original Columbia Scale	33.7%
Sleepiness	Item of original Columbia Scale	31.0%
Work Performance	Additional item (derived from WHO-HPQ)	19.4%
Alertness & oncentration	Additional item	22.9%
Vitality	Combined measure from SF-36	28.4%
Mental Health	Combined measure from SF-36	13.9%

Although not reaching statistical significance after Bonfer-roni correction, between group analysis of self-reported work performance over the 3 months of the study showed a sizeable positive trend in favour of the intervention. Within group analysis yielded an almost 20% increase in mean work performance score in the intervention group, with only marginal changes seen within the control group, suggesting this area would warrant further exploration in future studies.

Discussion

The present study is the first to investigate the ability of newly developed 17000 K fluorescent lights to achieve non-visual, biological effects within a workplace setting. Despite having had a relatively large number of participants compared to existing research in the field, the total number taking part in the study was still small. This, together with the fact that there was an uneven distribution of subjects in the two experimental groups makes drawing firm conclusions difficult. If the control arm of the study contained a greater number of individuals it is possible that the within group analysis for this group would have yielded more significant results, akin to those seen in the intervention arm. Certainly the direction of observed changes within the control arm was often in the same direction as that seen within the intervention arm.

Table 5. Trouble concentrating or thinking clearly at baseline, week 7 and week 14 by group. Mean score derived from the Columbia Scale according to response to the second question, "Over the last 3 days how much have you been bothered by trouble concentrating or thinking clearly? Possible answers and scoring: 1 = not at all, 2 = a little bit, 3 = moderately, 4 = quite a bit, 5 = extremely.

Time point	Control (n = 23)	Intervention (n = 46)
	mean score (SD)	mean score (SD)
Baseline	2.5 (1.1)	2.9 (1.2)
Week 7	2.6 (1.1)	1.9 (0.9)
Study end (Week 14)	2.5 (0.9)	1.8 (0.9)

A further consideration is that this was not a fully blinded study. Although participants were not explicitly told to which group they were assigned, feedback indicated that the lighting differed visually between the two floors. There is hence the possibility of biased responses to questionnaires by those on either floor and cross contamination of information between the groups. There is also a possibility of bias in responses due to the Hawthorne effect [22,23] and indeed, the placebo response is well recognized within lighting studies. [24,25]. Although every effort was taken to ensure study participants were not influenced as to the possible outcomes of the study, this cannot be fully discounted. As it is not possible to quantify the extent of such bias, any difference in the relative improvements of indicators between groups must be interpreted with care. This having been said, this was a 'real world' study designed to ascertain whether the positive effects of high correlated colour temperature lighting observed in a more controlled environment could be translated to the workplace.

Of note, our sample differed at baseline in a number of SF-36 measures from a general US population. [21], with a tendency for lower scores on some of the scales indicating poorer self-reported health. This modest difference is not unexpected, given the shift working nature of study participants, and serves to highlight the health and well-being issues experienced by shift-workers in call centres.

Since the study was conducted from February to May, some of the improvements observed may be attributable to seasonal effects, associated with the lengthening of days during the transition from winter to spring. There were indeed improvements observed in both groups for a number of measures, and improvements in the control group may provide an indication of the magnitude of the seasonal effects on the measures collected here. However, it is reassuring that there was a statistically significant difference between groups for a key measure at study end, which can reasonably be attributed to the effects of the intervention, beyond any seasonal effects.

It is encouraging that findings indicate improvements in a number of self-reported measures including aspects relating to concentration, alertness and energy.

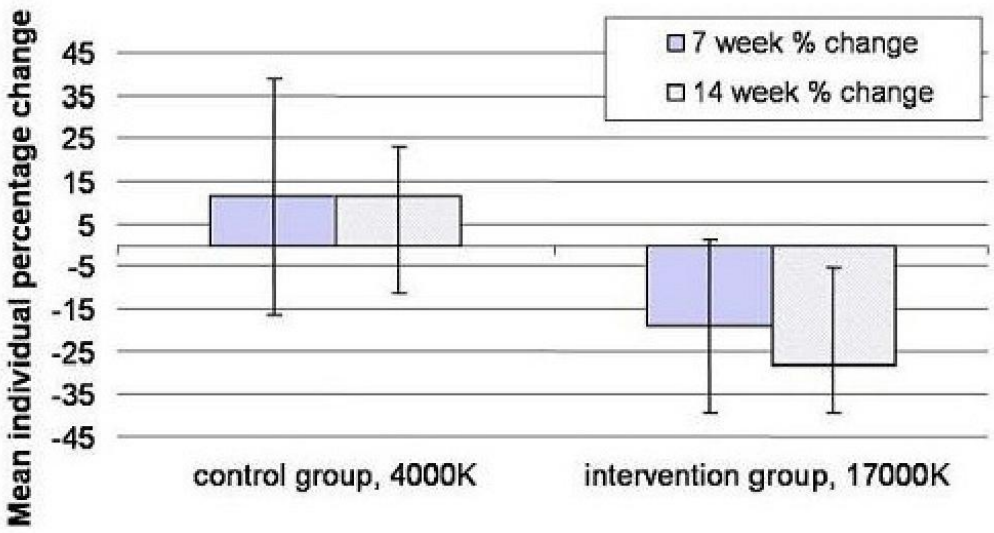

Figure 2. Percentage change in reported 'trouble concentrating or thinking clearly' during the preceding 3 days.
The plot shows data from 7 and 14 weeks after baseline in control and intervention groups (error bars represent 95% confidence interval for the mean change).

It appears that the lights contributed to general feelings of well-being, which may plausibly have led to the observed self-reported improvements in work performance. For the duration of the study SLH provided weekly group call handling data for both floors, and although this was not individual-specific, and hence not amenable to robust statistical analysis, it did show a modest improvement in the proportion of incoming calls answered from week 9 until the end of the study in the intervention group as compared to the control group (0.53%) which within the context of a large call-handling centre could lead to significant improvements in customer satisfaction.

The present study did not investigate the effect of the light intervention on the sleep quality of participants directly;

however, it is possible that some of the observed effects were associated with an improvement in sleep quality. Exposure to bright light during the daytime has been reported to enhance nocturnal melatonin levels [26,27] and improve sleep [28,29] and although the present study did not use bright light conditions, the larger amount of short wavelength light in the high correlated colour temperature light sources used for the intervention may have resulted in an ambience more analogous to the lighting conditions outdoors. It is certainly feasible that compared to conventional light sources, lamps with enhanced short wavelength composition may be used to reduce the light levels needed for achieving biological, non-visual effects so that these effects can be realised in an energy efficient way. With greater awareness of environmental issues and energy consumption globally, this is an area that should be investigated further.

Feedback from study participants indicated that the new lighting was well tolerated, compared with the standard lighting, and was preferred by the majority of individuals. Most pertinently, feedback indicated that the majority of participants on the intervention floor (41 of the 46) wished to keep the new lights at the end of the intervention period. The specific wellbeing effects of the new lighting found in this study probably

explain, at least in part, the high acceptance of these lights.

The questionnaires used in this study are not specifically designed to evaluate the effect of lighting interventions in the workplace; however, certain individual questions reported in this paper appear informative in this context, and on this basis we would recommend questions from the Columbia Jet Lag scale, and a selection of the scales from the SF-36 questionnaire, for future evaluation of lighting conditions.

Knowledge about potential health and well-being related benefits of light has led to an understanding of the need for indoor lighting strategies that are optimal for vision and human physiology simultaneously. Exposure to the new generation 17000 K industrial lights in a call centre in Stockport resulted in positive trends observed across a wide range of wellbeing and functional status variables, as compared to a control population, as well as a significant improvement in reported ability to concentrate.

Conclusion

The installation of new high correlated colour temperature (17000 K) fluorescent lighting in a shift-working call centre appears to have contributed to wide ranging improvements in wellbeing, functioning and work performance amongst study participants. The lighting is well tolerated and has the potential to be a cost-effective means of impacting upon employee wellbeing and productivity.

Further studies are needed to quantify the observed effects in larger and different working populations.

Abbreviations

SF-36: Short Form 36 Questionnaire

WHO-HPQ: World Health Organisation Health and Work Performance Questionnaire

SLH: Standard Life Healthcare

Competing interests

LS is an employee of Philips, which provided the lights for the study.

Authors' contributions

PM developed the study protocol, collected the data and contributed to data analysis and writing of the manuscript.

ST analysed the data and contributed to writing the manuscript.

LS organised the follow-up of the lighting intervention and contributed to data analysis and writing of the manuscript.

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REVIEW OF BLOODLETTING AND MIRACULOUS CURES BY VINCENT LAM

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Few first books are fortunate enough to receive both high praise and big awards, but Vincent Lam's *Bloodletting and Miraculous Cures* deserves the attention. Celebrated by critics and awarded one of Canada's top literary prizes, *Bloodletting* is a masterful, smart and engaging debut collection of short stories. Part-time writer and full-time emergency-room physician in Toronto, Vincent Lam paints a three-dimensional portrait of physicians grappling with inner struggles, ethical dilemmas and hospital-room obscurities. The collection follows four Toronto doctors – Ming, Sri, Fitzgerald, and Chen – from hopeful undergrads to medical trainees to seasoned physicians. Through their experiences, Lam examines the myths and truths of today's health care world.

The collection's four main characters are, in the end, practicing physicians, and "practicing" is the key word here. The doctors in *Bloodletting* practice medicine; they do not perfect it. They guess at the effects of their actions. They try to interpret symptoms, reach infallible conclusions, maintain their authority, and care for their patients. But they make mistakes. They argue. Sometimes they hate their work. It is that recognition of the difficulties of providing health care that makes this collection enjoyable and important. *Bloodletting* succeeds because it challenges the myth that doctors are omnipotent and medicine is objective. Instead, this book offers a complex rendition of hospital life, one that is simultaneously valuable for its literary merits and relevant to the field of bioethics.

Opening up Bloodletting

Lam's complex rendition of medicine, hospitals and doctors makes the collection appealing for all kinds of readers, from those who cannot tell a crash cart from a cardiogram to health-care insiders who may well recognize their own experiences on the pages of *Bloodletting*. For instance, in "How to Get into Medical School, Part 1", we are introduced to Ming, a no-nonsense and meticulous undergraduate student. She has finished her molecular biology exam characteristically early but is lingering to time her exit from the classroom with Fitzgerald, the artistic study partner with whom she has shared many late nights in the library. Their romantic, post-exam exchange in which Ming gushes to Fitzgerald, "Thank you for explaining the Kreb's cycle to me," will bring a smile of recognition to those for whom undergraduate crushes have developed in the depths of library basements – and for those who have endeavoured to learn the Kreb's cycle.

In "Take All of Murphy", we enter the anatomy cadaver dissection lab, which Lam describes as the "first rite of medical school". We are introduced to Sri, "the sentimental wreck who can't even cut open an arm", and his classmate, Chen. Here, our medical students are confronted with the first of many ethical dilemmas presented throughout the stories. In this case, the students argue over whether or not to cut through the biblical scripture text tattooed on their cadaver. "You should respect a man's symbols", says Chen in response to Ming's insistence that they adhere to the dissection instructions. This is the first of many instances whereby cut-and-dry rules collide with nebulous real-world situations.

By the seventh story, "Eli", our characters are now physicians. Fitzgerald is a trauma doctor juggling a chaotic emergency room when two police officers arrive with their arrested suspect, Eli. He requires medical care for a head wound that is likely the result of police brutality. In this story, Fitzge-

rald, who was gentle and sincere as a medical student, has transformed into a shrewd and forthright adversary within a system of power struggles. "The game is supposed to go like this", he tells us, by way of introduction to the manoeuvring of various authority figures in his ER. Eli is a physical threat, but it is the police officers whom Fitzgerald approaches with the most cunning and suspicion. Once again, Lam removes the crisp white lab coat from the profession and gives us a view of medicine as marred and, to some extent, unheroic.

By the time we reach "Night Flight" near the end of the collection, Fitzgerald has developed a substance addiction. As a result, he has been forced to leave his position at the hospital and is now employed as a travel physician, a line of work in which he can keep his addiction hidden. However, Fitzgerald's substance use is the least of the ethical concerns raised in this story of a woman attempting to med-evac her dying husband from Guatemala to Canada. Additionally, we are introduced to conflicts between public and private health insurers, rich and poor country medical capacities, and hurtful truth-telling versus compassionate lying.

Bloodletting in cultural and literary context

Throughout these and his other stories, Lam paints a picture of physicians as well-intentioned, partly-competent masters of illusion. They are men and women who hold the pose of confidence and certainty without always possessing it. Their authority, knowledge, and apparent control of the situation are often manufactured to serve professional and, occasionally, personal ends.

For those reasons, the last story's final image functions as a metaphor for the entire collection. After a tiring and frantic night shift in the emergency room, Chen returns home to a darkened bedroom: "The light through the blinds falls diagonally in fat stripes on the floor, and is warm on the carpet whose stains are highlighted and made attractive, important." In Lam's collection, the stains and messes that characterize the practice of medicine are highlighted and made attractive, important. It is the doctors' foul-ups, the valiant attempts, the guesswork, and the emotional turmoil that are made important here, not their enlightenment, their objectivity, nor their cold, clinical perspective.

This version of medical science and its practitioners is crucial and sets it apart from other contemporary renditions that celebrate doctors as infallible knights in shining white-lab-coat armour and science as completely reliable and failsafe. In short, *Bloodletting* is the anti-*CSI*. Whereas the TV-series *CSI* (*Crime Scene Investigation*) presents science as unambiguous, unquestionable and objective, *Bloodletting* reminds us repeatedly that medicine is an inexact science full of guesses that go wrong, messes that are beyond cleaning and problems that cannot be solved with a quick stitch or pill.

Lam foreshadows this idea with the quotation that introduces his collection – "Medicine is a science of uncertainty and an art of probability" – and reinforces it with a glossary of over one hundred medical phrases at the end of the book. Readers unfamiliar with these technical terms may find that their regular reference to this glossary through his early stories fades away as such details become unimportant to the actual challenges being faced by Ming, Fitzgerald, Sri and Chen. The more that we view these medical tools and diagnostics as irrelevant, the more we encounter physicians who are illusionists drawing on a very different set of talents with which to manage scenarios. The glossary thus becomes ironic, signifying not the possibility of full and complete knowledge, but rather its absence and elusiveness.

Those are heady and important ideas and, to Lam's credit, he weaves them into immensely entertaining and compelling stories that have earned him the high praise that he deserves. In the context of popular versions of medicine or science, therefore, the collection is new and exciting. But in the context of Canadian literature, these ideas – the difficulty of objectivity, the trouble with

authority, the challenge of so-called clear communication – are familiar ones, already examined with significant complexity by a long line of well-recognized Canadian authors: Mavis Gallant (in her From the Fifteenth District stories), Alice Munro (in Lives of Girls and Women and beyond), and Margaret Atwood (in her Bluebeard's Egg and Wilderness Tips collections). Because these more accomplished authors have already covered similar ideological territory, on occasion Lam's stories appear to be lighter and simpler (but more accessible and more entertaining) versions of their predecessors. "Code Clock," for instance, is a great story, but its conclusion is too quick, too cute, and (almost) too didactic. "An Insistent Tide" suffers a similar fate. But that occasional simplicity alone is not enough to disapprove of Lam's collection; the fact that the comparison to literary heavyweights like Gallant, Munro, and Atwood can be made at all is a tribute to Lam's accomplishment.

Bloodletting as a tool for bioethics training

Along with its literary contribution, *Bloodletting* also has relevance for academic training. Lam's presentation of health care as messy and subjective parallels the messiness of bioethics. While there are clear-cut right and wrong answers to some questions, much of bioethics involves the search for solutions that are most right or least wrong, positions that can change with a shifting point of view. To this end, Lam's stories might find themselves a home in bioethics curricula as training tools. The initial step in ethical decision making is recognition and articulation of issues as moral dilemmas in the first place. Each of his short stories is embedded with ethical quandaries that could act as a springboard for such bioethics teaching.

In "Code Clock", for instance, we see our medical resident responding to a "code blue" for a hospital in-patient with a cardiac arrest. This is a tense and compelling story during which we have access to the resident's inner monologue. His failing confidence and capacity will prompt many readers to consider avoiding teaching hospitals in the future. However, Lam has hit on a real and central challenge in medical training: how to balance the inevitable need to learn new skills with the dire risks associated with incompetence. This story points a spotlight on the medical school mantra of "watch one, do one, teach one", prompting critical reflection on the process of becoming a proficient practitioner. The story is also imbued with counterproductive power dynamics amongst the various physicians and nurses at the scene, providing yet another starting point for ethics discussion with health care trainees.

In "Winston", Lam presents Sri as a medical trainee providing a psychiatric consultation for a young man who believes he has been poisoned. Readers join Sri in his journey from clarity of purpose at the start of the encounter to self-doubt about what is real and what is right by the end of the exchange. Lam gives bioethicists much fodder for discussion. First, he prompts us to consider the challenges associated with judging patients' truthfulness in the face of possible psychosis and, moreover, the consequences of being wrong. Second, in this story and others, he encourages us to question what constitutes appropriate supervision of medical trainees from their overseeing physicians who may be distracted, disinterested or themselves ill-informed. Most important, however, is the issue of boundaries in medicine and the lengths to which health care providers can and should go to provide appropriate care.

Sri's unease with the situation prompts him to step outside of typical behaviour and visit Winston's home where his understanding of the story becomes even more confused. Sri's actions, born from care and concern for Winston's welfare, ultimately lead to a situation of violence and harm for his patient. This story lays bare the conflict of dual loyalty faced by health care providers; that is, commitment to their patients on one hand, while simultaneously acting as society's gatekeepers in line with legislation (in many environments) that authorities be alerted if a

person presents a danger to him/herself or others.

"Contact Tracing", a topic of perennial interest to bioeth-icists, is the title of one further story that provides rich material for ethics training. Here, Lam draws on his experience as a Toronto-based physician during the SARS epidemic in 2003. Supported by World Health Organization press releases and fictitious medical chart entries, Lam presents the experiences of a range of physicians and nurses as they struggle through this devastating experience. His characters suffer the stigmatization of quarantine, the dehumanization of isolation and the sequelae of SARS itself. He describes the impact of one hospital's strategy for selecting and then compelling nurses to serve on their new SARS unit, prompting contemplation amongst readers on health care providers' duty to care and just reciprocity for such service. Like much of this book, "Contact Tracing" is accessible to all but will have a unique impact on those who can associate with the experience – in this instance, a health care response during an infectious outbreak.

Conclusion

"Dignity and decorum are crucial", says the anatomy instructor in "Take All of Murphy", but they can be difficult to achieve in Lam's world of health care. Accuracy, objectivity and precision are also crucial, but in this collection they, too, are elusive.

Bloodletting and Miraculous Cures offers a refreshing, entertaining and sometimes disturbing view of doctors and doctoring that is satisfying to both readers unacquainted with the challenges of medicine and those all too aware of the messy reality of the practice. It is a credit to Lam who uses his imagination and, no doubt, his experience as an emergency room physician to cut beneath the surface and present a collection of stories that brings to light the everyday quandaries faced by health care providers.

CHEMICAL COMPOUND RL – 175 – A BREAKTHROUGH IN CONTEMPORARY THERAPY OF DISSEMINATED PROSTATE CANCER

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At present medicinal effect of disseminated hormone dependent prostate gland cancer (DPGC) therapy includes medical castration in combination with antiandrogen application. However the effectiveness of blocking both testicular and adrenal antiandrogen production is little and this does not lead to the DPGC recovery. The average duration of the response to hormonotherapy does not exceed 18 months and the effectiveness of chemotherapy comprises only about 9 %.
In this paper we present the experimental and clinical results of 10 DPGC fatal cases therapy by chemical preparation RL-175 developed by the author. As a result these patients at $T_4N_1M_{1-3}$ stage have been brought to nearly complete tumor remission, to both subjective and objective stabilization of tumorogenic process for 3 and more years. The conception is being discussed of both overcoming and blocking the development mechanisms of this tumor hormonotherapy and chemotherapy resistance under the effect of RL-175, as well as the fundamental possibility of the widest possible use of RL-175 with the preventive purposes.
Key - words: antiandrogens; preparation RL-175; disseminated prostate gland cancer; medical castration.

Introduction

For the last years considerable success in formation of new therapeutic methods and clinical diagnostics of prostate gland cancer (PGC) has been achieved. First of all it regards the results of the European cooperative randomized investigation [l] and the American oncologic group [2-4] as well as [5, 6]. It follows from these papers that nowadays androgen deprivation is one of the most prospective ways of the treatment effectiveness increase of patients with locally invasive PGC. Androgen deprivation includes surgical castration (total or subcapsular orchiectomy) or medical castration. Orchiectomy is considered to be a standard regarding which medical castration is assessed. The latter method includes the use of two preparation groups: estrogens and RH-LH analogues (diethylstilbestrol, gozereline acetate, leuprolide acetate, treptoreline, busereline and others). One kind of castration presupposes the administration of antiandrogens - flutamide (eulexin) and bikalutamide (casodex).

Medicamental castration objectively lowers the level of testosterone to the orchiectomic effect. However these generally accepted methods manifest considerable side effects. Even if they are still relatively effective in the treatment of $T_3N_0M_0$ stage patients, they are not accepted at all with the DPGC ones.

According to the growth rate PGC takes the 2-nd place after melanoma. Among male death causes PGC takes the 2-nd place after lung cancer. When tumor is localized a radical prostatectomy is indicated. However by some data in 50% of cases recurrence follows it [5,6]. In spite of the state programs of PGC early recognition in the developed countries the tumor is detected on the III-IV stages in the most of patients (61%). The absence of such a program in Russia has led to the fact that up to 80% of PGC patients during their primary inspection have already had remote metastases [7].

Thus the DPGC treatment is the most complicated problem. The average life span of PGC patients after surgical and medical castration in the combination with antiandrogens does not prevail 18 months [8], and the effectiveness of chemotherapy regimen of PGC hormone-resistant patients is 9% [9].

On the other hand well-known methods of therapy are not accepted or are of little use in PGC prophylaxis. It seems(it is obvious) that without wide prophylaxis of the population PGC will remain a vital issue for the future. In this connection the searching of new preparations and ways of PGC treatment is

topical. Our work is focused on the attempts to solve the problem.

Patients and Methods

By the authorization of the Ministry of Public Health of Russia № 10-13, July 21, 1991, ten fatal cases aged 50-66 (average age - 58) having the morphologically and cytologically verified diagnosis as PGC of the $T_{3-4}N_1M_{1-3}$ disease stage were picked out for the approbation on a voluntary basis.

Prior to the experiments all the patients had undergone a complete course of the up-to-date therapy. In all the ten cases the said course of treatment had either very little or no effect at all.

RL-175 was administered to all the said patients every day orally on an empty stomach during 30 days. The daily dose of the preparation was 15 mg dissolved in 10 ml of the fruit syrup or in the physiological salt solution.

RL-175 is a heteroaromatic compound. Its physicochemical and biological properties are described in [10].

The preparation effectiveness evaluations after the treatment course completion were: the finger test of the prostate gland; ultra-sound test; the computer tomography and the patient life span after the latest unfavorable prognosis for the disease.

It should be taken into consideration that these ten patients lived in various towns of Russia, all of them were examined and treated in different oncological hospitals. That's why the author couldn't have all the official protocols proving the real effectiveness of the monotherapy with RL-175.

The present article contains the official conclusion of the oncologic dispensary № 4 from the Health Department of Udmurt Republic (Russia). It can be taken as an objective averaged conclusion for ten patients.

Patient S.(1928), a pensioner, lives in Izhevsk, Udmurt Republic (Russia). First he turned for help to the oncological dispensary №4 in Izhevsk in 1988. Based on the biopsy of the prostate gland № 687-88 and № 689-90, the specialists diagnosed the acinose adenocarcinoma with the discomplexation and the far metastasis.

After the general courses of the hormonotherapy and chemotherapy in the III Central Administrative Board of the Ministry of Public Health of the USSR the patient's state improved and the metastatic centers in the bones disappeared. In November 1993 the patient's state sharply became worse. The patient had strong pains in his back, he stayed in bed, lost weight and felt worse. Scintigraphy of the skeleton bones showed the metastases in the area of IX-X ribs on both sides. He also had up to 40% of the bone metastases in the area of the pelvis bones and other places.

The secondary examination of the patient S. in November - December 1993 confirmed the first diagnosis: the prostate gland cancer of $T_4N_1M_{1-3}$ stage with the metastases into the spine and ribs, into the iliac area and possibly into the urinary bladder. With the help of the rectal counter the tumor size was determined as 5.4-5.1cm. The doctors evaluated the patient's state as critical with the nearest unfavorable prognosis.

Then the patient was treated with 4 monotherapy courses based on the preparation RL-175 with the short breaks between the courses. The first course started on February 10, 1994 and lasted till May 10,1994.

Dependence of including [^{3}H]-thymidine, [^{3}H]-uridine and [^{3}H]-L-leucine into the cell of human ovarian carcinoma line from concentration of preparations RL-3, RL-175 and RL-S was made by radiometric method [11]. The results are set out in Fig. 1 (a, b, c).

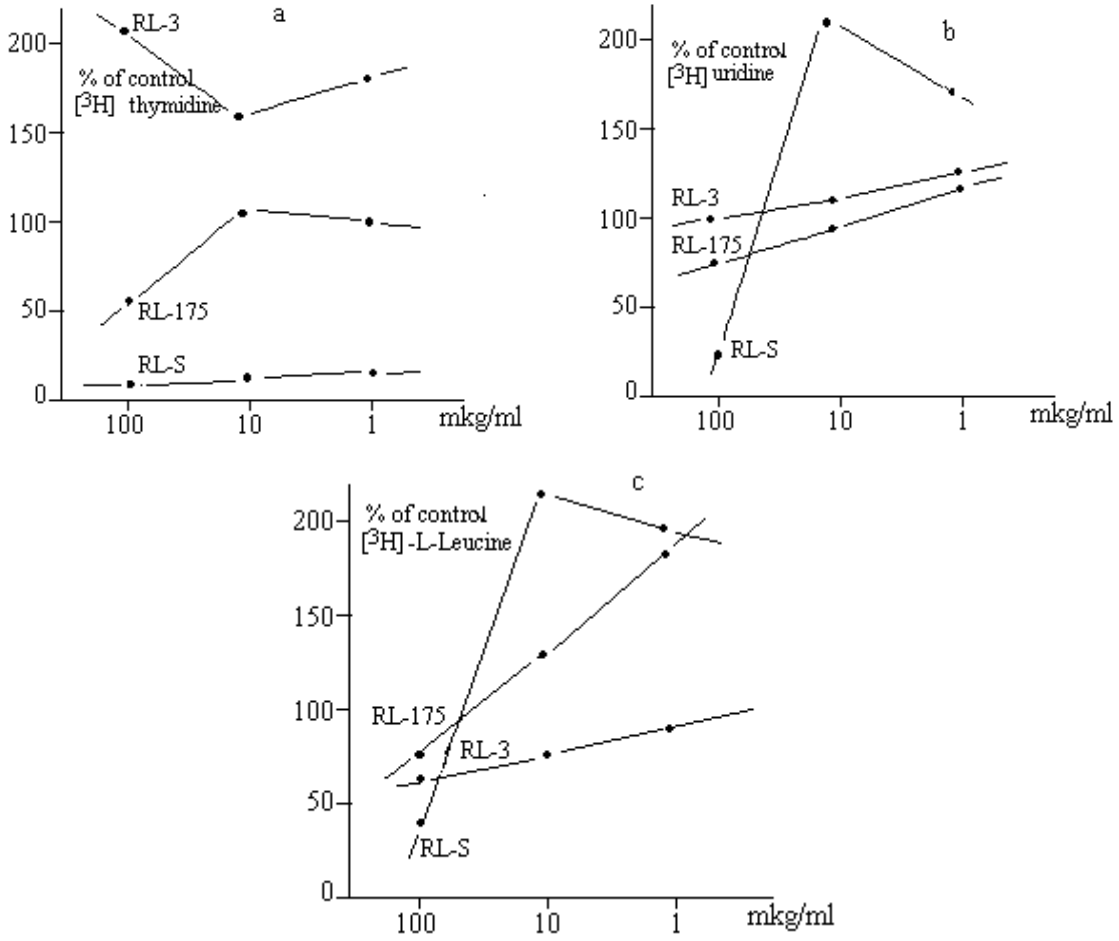


Figure.1. Dependence of including [^{3}H] – thymidine (a), [^{3}H] – uridine (b) and [^{3}H] – L-Leucine (c) into the cell of human ovarian carcinoma line from the concentration of preparations of RL series.

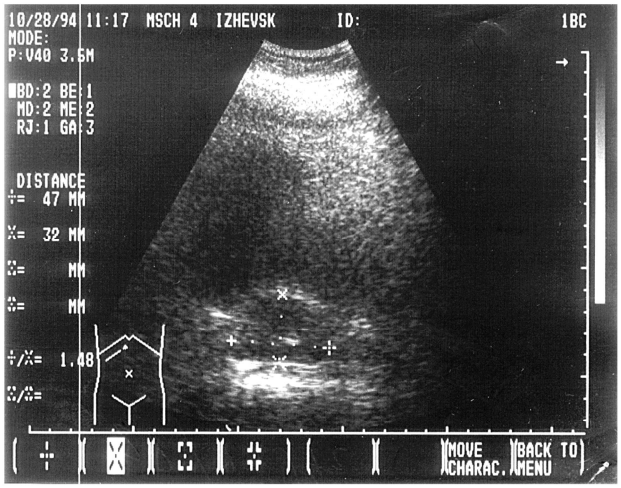
The data resulting from the studies, were processed by using variation statistics Student's t ratio.

Clinical investigations on human subjects were correct in compliance with generally accepted ethic and moral principles in correspondence with the Declaration of 1964 and 1995(revised in Edinburgh, 2000). Into the clinical approbation fatal cases were included on a volunteer basis**.** They gave written consent.

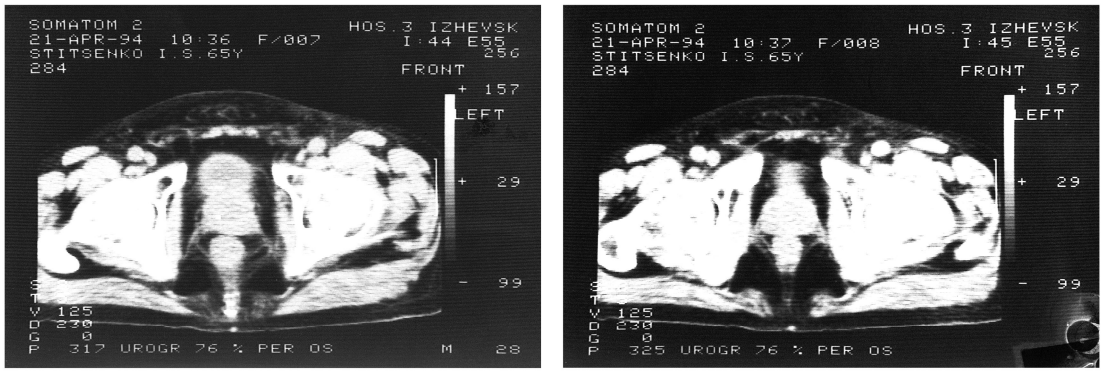
Results

The computer tomography held on April 21, 1994 showed: after the first course of monotherapy on RL-175 there was a moderate decrease of prostate gland in 35x44x50 mm (tumor regression for about 50%); the front contour wasn't clear, closely connected with the urinary bladder, its walls were infiltrated (Fig.2). The computer tomography comparative analysis of the abdominal peritoneum cavity and the small of the back (April 21, 1994 and February 22, 1996) didn't show the negative dynamics of the tumor increase.

The U-sound diagnostics results on September 28, 1994 (Fig.2) showed the gross section size of the prostate gland - 47mm, front-rear area - 32mm the contour was rough, the structure was diffusely nonuniform.



a



b

Figure 2. The upper fig.(a) –U-sound diagnostics of the patient's prostate after 8 months of the RL-175 reception beginnings (tumour size 47x32 mm). The tumour size according to the rectal counter were 54x51 mm prior to the preparation reception. The fig.b – the computer tomography of the prostate after the first course of monotherapy on RL-175 (35x44x50 mm) negative dynamics of the tumour growth was not revealed since 04.21.1994 to 02.22.1996.

Now the patient's general state is quite satisfactory. He is active, has a good appetite, drives a car, goes fishing.

From the very beginning of RL-175 reception the full blockade of the pain has taken place. The examination period is 48 months.

In the experiment we showed that preparations under the code RL-175 accelerate, on 60-80% ($P<0,01$) the oxidation of succinate by rat mitochondria ($1.14x10^{-6}$ mole•s against $0.67x10^{-6}$ mole•s in control) what is adequate at the same time to the acceleration of phosphorylation of ADP in ATP ($ADP+P_i \rightleftarrows ATP$) [12]. By the method of qualitative thin-layer and gas-fluid chromatography there also was revealed increase in vivo in skeletal and cardiac muscles of experimental rats fed by RL-S and RL-175, synthesis ATP up to 3 times regarding control indices.

However by that veritable free energy (ΔG) of ATP hydrolysis in pointed cells of muscles by concentration of ATP, ADP and

P_i correspondingly 40, 0.93 and 8.05mM and significance pH 7.0 and 25° C did not increase ΔG discharged at hydrolysis of energetic value in intact erythrocytes, muscle and rat's liver [13]:

$$\Delta G = \Delta G^{01} + 2{,}303RT \lg \frac{[ADP][Pi]}{[ATP]} = -51{,}9 kj / mole$$

where:ΔG^{01} – standard free energy; R – gas constant;
T – absolute temperature and P_i – phosphoric acid.

With the account that synthesis of one molecule ATP from ADP and P_i is carried out in standard thermodynamic conditions - 30.5 kj/mole, then the difference in – 21.4 kj/mole comprises the standard energy (ΔG^{01}) of displacing the preparations RL of the mentioned above balanced system (K_b) in the pool of multifermental complex of respiratory chain in 10^{10} times regarding the balanced (K_b°) uninvolved spontaneous passing of molecule A into B K_b° = $1.15x10^{-3}$;

$$K_b = \frac{[B]\cdot[ATP]}{[A]\cdot[ADP]\cdot[Pi]} = 0{,}28x10^{7},$$

where: for A spontaneously turning into B by G^{01} = - 21 .46 kj/mole
$K_b = 5.62x10^3$, ratio [ATP] / [ADP][P_i] is equal to approximately 500.
Apparently under the influence of RL in 3-key points of respiratory

$$NADH + H \rightarrow \overset{area\,I \uparrow ATP}{\overbrace{E-FMN \rightarrow [F_e - S]_n}} \rightarrow \overset{area\,II \uparrow ATP}{\overbrace{Q \rightarrow b \rightarrow C_1 \rightarrow C}} \overset{area\,III \uparrow ATP}{\overbrace{\rightarrow aa_3 \rightarrow o_2}}$$

chain not three but four molecules are synthesized. We should take into account that equilibrium constant K_b° in the chain is being displaced 10^{40} times, it is considerably higher than the physiological norm in regard to control which is 10^{24} times [13]:

$$ADP + Pi \underset{RL\text{-}175}{\overset{10^{16}\ times}{\rightleftarrows}} ATP$$

In addition to the outstanding bioenergetic function of ATP (moving, active transport, biosynthetic metabolism) one more function is known that is amplification (strengthening) of impulse [13]. In the response to the action of some polypeptide hormones, risk factors, mitogens and cytokines (endogenic irritators) on plasmatic membrane of the animal cell in anaerobic conditions ATP from ADP and Pi is synthesized.

The displacing by the preparations RL-175 and RL-S of thermodynamic equilibrium constant ADP + $P_i \rightleftarrows$ ATP in 10^{16} times in regard to the physiological norm is associated with the considerable synthesis of ATP in the plasmatic membranes of malignant cells in regard to ATP zero concentration in neoplasia [14]. The ATP energy increase in the plasmatic membranes of malignant cells becomes again accessible to the endogene receptors, particularly for the insulin receptors [14,15]. This provides the cascade of mechanisms starting, mechanisms of the cell ingress in to the nornal cycle of the cell proliferation via tirazine kinase receptors activation and via other factors.

Structural dependence of the investigated compounds on the synthesis of DNA and RNA based on inclusions of [^{3}H] - thymidine on [^{3}H] - uridine into the cell of human ovarian carcinoma CaO_Y line was revealed. For example, under the RL-3 influ-

ence synthesis of DNA decreases twice when the dose of preparation is 100 mkg/ml (fig. 1 a, b). This effect of RL-3 on the DNA synthesis is persistent even in case of low concentrations.

Preparation RL-175 in the dose 100 mkg/ml makes partial inhibiting influence on the inclusion speed [^{3}H] - thymidine. Synthesis of DNA increases in doses 10 and 1.0 mkg/ml of the mentioned preparation. In its turn RL-S practically wholly inhibits DNA synthesis and at the same time considerably stimulates RNA synthesis: inclusion [^{3}H]—uridine in the dose of 10 mkg/ml on 214% regarding on the control index.

On Fig. 1c there are presented the data of RL-series preparations influence on the inclusion rate of [^{3}H]-l-Leucine into the cells of human ovarian carcinoma kind. It results from the data that protein synthesis corresponds to the proliferation rate.

Discussion

At present when treating metastatic PGC a number of cytostatic agents (metoxantrone, estramustine, docetaxele, vinblastine, vincristine and others) is used. A therapeutic target for them is Bcl-2, P-glycoprotein, topozomeraze, cytoplasmatic tubes and others. Active search for effective antibodies and rational combinations of drug dosage regimens is being carried out [16].

Specialists hold to the same opinion that the key role in hormonal and chemical resistance of this tumor belongs to genes and antigens controlling apoptosis: p53, PTEN, Bcl-2 and others [15,17-19].

The sensor of DNA damage and cellular cycle damage is gene 53 that codes nucleus protein with molecular mass 53 kD and is able to initiate 2 programs independent of each other:

- temporal failure of cellular circle in G_1S-phase by means of protein p21 inhibiting cyclyne-dependent kinases [17];
- stimulation of apoptosis by the activation of Bax or Bid of Bcl-2 family genes. Pro- and anti-apoptotic action of activated proteins of Bcl-2 family is achieved via the modulation of mitochondria activity.

From the above mentioned experimental and clinical material it may be concluded that under the influence of RL series preparations there takes place a reverse in the mechanisms of the mutarogenic cell ingress into normal mitotic cellular proliferation cycle. The ratio of phases of this cell mitotic cycle $MG_2 > G_1S$ is the measure of gene p 53 activation.

The exclusive role in the apoptosis [15] starting belongs to mitochondria as opposed to hypothesis [20]. Apparently under the influence of RL-175 the apoptotis signal ingress into the nucleus increases parallel with ATP from ADP synthesis growth. The activation of nucleus gene P53R2 that codes the ribonucleotidreductase is achieved in this way. This enzyme is responsible for reparation of mutated DNA.

In the cases, when for some reasons DNA repair is impossible, a cascade of apoptosis mechanisms is started/activated very quickly. This process is accompanied by the outflow of cytochrome c, ATP, Ca^{2+} apoptosis-inducing factor into cytozole via metachannels due to the Bcl-2 family protein activation. Cytochrome c activates caspase 9 which in its turn activates killer caspase 3. Thus the signal way of apoptosis caused by DNA impair is finished.

Thus the possibility of gene p53 activity correction up to the norm and starting the apoptosis mechanisms via family Bcl-2 gene activation under the preparation RL-175 influence is a serious factor in overcoming the resistance barrier of this tumor to hormonotherapy and chemotherapy. If the average DPGC patients life span is rather low, then a 4-year almost complete remission of 10 fatal cases of $T_4N_1M_{1-3}$ stage is evidence of the near victory in the fight with this severe disease.

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ANION EXCHANGER OF ERYTHROCYTES MEMBRANE (REVIEW)

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Erythrocytes membrane representations as fiber lipid complex are well-known, they have been included into school textbooks. Now the basic tendency of molecular membraneology and cellular physiology is to disclosing separate components of a cellular membrane and providing of normal functioning of a cell in its interrelations with an environment. In the review the modern condition of question on structure and functions of one of integrated fibers of a cellular membrane identified as fiber of strip 3 (f.s.3) with the help of electrophores is considered. In erythrocytes of f.s.3 carrying out anion exchange, mediates carry H^+ inside of cell and serves as the active participant of transport CO_2 in blood of the person and animals.

Structure of anionexchanger

Human f.s.3 is a part to the multigenic family of related fibers including three isoforms F.s.3 of erythrocyte membrane membranes relates to isoforms AE1, functioning. AE2 – anionexchanger presents in tissues. AE3 is expressed with the cells of heart, brain and retina tissues [5,13].

AE1 of person erythrocytes is glychosilire membrane fiber with molecular weight 110 consisting of 911 amino acids [21]. There are two 2 functionally differing domains in it: C-terminal, penetrating into membrane, and N-terminal, M=40, exhibited on its surface [3, 27, 33].

The analysis of cloned AE1 has shown significant homology of its trance membrane domains at various kinds of animals. The all consist of 10 waterproof regions penetrating membrane at least in 12 times. The N-terminal domain, on the contrary, showed divergence during evolution. Only responsible for linkage of ankirin the fragment of this domain is homologues among AE1 of different kinds [20].

In particular, transmembran domain of erythrocyte anion exchanger of chicken is more than in 70 % homologues to domains of f.s.3 of other kinds [7]. The waterproof part of molecule penetrates the membrane in 12-14 times. The majority of the amino acids directly participating in carry anions are conservative. On the other hand in N-terminal domain about 90 amino acids of human and rat f.s.3 are absent, as a result there is no site of linkage gliceraldehyde -3-phosphatdegidrogenase. The other part of cytoplasm domain is only in 40 % similar to N-domains of other kinds though the ankirin connecting region is conservative [7].

By means of antibodies to various sites citoplasmatic domain f.s. 3 it is shown [20], which sites of linkage of ankirin are localized at cistein cluster 21-317 and in N-terminal area citoplazsmatic domain that specifies presence of 2 various sites citoplazsmatic domain AE1, on primary sequence is far from each other [34].

The famous aspect, concerning structures of this fiber is its oligomer condition. AE1 can be covalent connected in diameters and actually in a membrane, presented as a mix of homodimers and homotetrametres [27]. Only after denaturation by dimetilmalein angidrin or SDS anionexchanger of membranes passes in the monomeasured form. Ankirin is connected, basically, with teramers AE1 [30]. This conclusion follows from data on anisotropy of fluorescence in which existence of 2 populations AE1 - is proved to one with smaller molecular weight, more mobile, another - with greater, immobilized [30].

Functions of anion exchanger

Each of two domains AE1 carries out strictly certain functions. For transport of anions is responsible C-terminal penetrating membrane area. Process of carry of ions is electrically neutral, owing to it transport CO2 by blood and stabilization pH plasmas is carried out [7, 15, 34]. In actually anion transport is involved a fragment of molecule P5, change of which causes proteolitic degradation of erythrocyte shadows. Here join all

known inhibitors of anion exchange (in particular at pH 7.3 – inhibitor of anion transport of phenilisotiocinat) [29].

AE1 transports small molecules of anions, including Cl-, HCO3-, H2PO4-, SO42- and others. Speed of exchange Cl- is constant at pH 7 11, hence, univalent anions are communicated under the transfer with guanidine group of the rest of arginin since only this amino acid has high value of pK and remains thus pH positively charged. For measurement of activity of ino exchange SO42 is often used which is transported in 104 times more slowly, than Cl-[31]. It is assumed, that with bivalent anions (SO42-, HPO42-) contransport H^+, unconnected from - ε-amino groups near to the rest of lisin [2, 20].

Speed of work of AE1 depends from pH and concentration of endocellular Ca^{2+}. Optimum for exchange oxalate/chloride value extracellular pH makes at 5.5. At alkaline values pH environments transport of anions are inhibited because of deproton of groups with pK 11.3 [20]. Ionophor AE23187, causing increase in concentration of endocellular Ca2 +, inhibits anion exchange [32].

AE1 mammals plays a critical role in system of transport CO2. In system capillaries CO2 on a gradient of paracial pressure diffunds in erythrocytes where turns in HCO3- which in turn leaves from erythrocytes in exchange for extracellular Cl-owing to work of AE1. Speed of such exchange is very high - the order 5*104 anion/s with - on this parameter this fiber is one of the fastest fibers-conveyors [1]. As quantity AE1 in a membrane is very great (1.2*106 spears/cells) [12], speed anion exchange for some orders exceeds speed of all other reactions participating in transport CO2.

Because of high permeability of membrane for anions, membrane potential of erythrocytes is according to transmembrane distribution of Cl.. Transport H^+ in эритроцит is carried out by reactions of cycle of Jacobs-Stewart [10]: in reply to extracellular loading acid H + incorporates to bicarbonate. H2CO3 is formed a coal acid which dehydrates up to CO2, quickly diffunding in erythrocyte inside of a cell. CO2 again hydrates up to HCO3 and H^+. Most part of H^+ is neutralized, and bicarbonate leaves the cell in exchange for Cl^- which acts inside of erythrocyte through anionexchanger. This phenomenon (хлоридный shift, by Hamburger), finishes the cycle.

N-terminal segment AE1 is not involved in transport of anions. Its removal does not break transport activity [20]. This region cooperates with ankirin, f.s. 4.1 and f.s. 4.2 [7, 13, 14, 34], forming sites of an attachment of a membrane to cytoskeleton. Owing to it the biconcave form erythrocyte [34] is supported. Hemoglobin, enzymes and glicolis also are attached to N-segment [16, 19], hemihromes which can cause aggregation of AE1 or change of the form of cells [4]. C-area of N-segment is connected with karboangidrase, forming methabolone, mediating carry of HCO3.[4, 31].

In old erythrocytes AE1 serves as an antigene, signal for their removal from blood channel [22]. It is also a receptor for invasion of *Plasmodium falciparum*. The mutation or deletion of a gene AE1 leads to occurrence of various variants of erythrocyte morphology and such diseases, as south Asian ovalocitose and erythrocyte spherocitose. Mice with insufficiency of AE1 have hemolytic anemia, growth and development is late, the percent if neonatale destructions [26] strongly raises.

AE1 also is responsible for group specificity of blood. Antigenes of Diego connected with dot mutations in its molecule (Di^a, Di^b, Rb^a, WARR, Wd^a). The changes of amino acids connected with last three antigens makes accordingly 548 Pro - Ley, 552 Thr - Ile, 557 Val - met [18].

If functioning of this fiber in denuclearized erythrocytes is investigated in details [8,9,10, 17] data about AE1 in nuclear erythrocytes of the invertebrates are not numerous [25].

In the membrane of nuclear erythrocytes all vertebrates except for Agnata also there is plenty of AE1, carrying out eletroneutral exchange Cl^- on ^{HCO3}.[23, 28].

Limiting step of transport of H^+ is non-catalised extracellular stage of dehydration of coal acid up to CO2. In comparison with a speed of anion exchange $t_{1.2}$ this reaction is in 100 times has less than exchange, than speed of anion exchange [28]. All steps of Jacob-Stewart 's cycle are passive. H^+ is distributed on both sides of erythrocyte membranes in conformity with value of membrane potential created by chloride.

Other mechanisms of carry H^+ in erythrocyte work only under special conditions. In [9] it is shown, that after degazing of environments reduction of concentration of H^+ occurs due to movement through membrane of H^+ or OH^-, kinetic characteristics of both types of transport are equivalent. Probably, stream of H^+, carried out on mechanism of N^+, Cl^- cotransport, dominates under sour values of pH, OH^-/Cl^- an exchange at alkaline.

Thus, successes in understanding of features of anion exchange between erythrocyte cell and the extracellular environment are rather significant. At the same time there is a big layer of problems which development depends not only the base of modern membranology, but also a lot of the practical problems connected first of all with clinic.

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HIERARCHIC MODEL OF AN ESTIMATION OF THE DOCTOR'S ACTIVITY ON THE BASIS OF INFORMATION TECHNOLOGIES

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In the article the questions of an estimation of medical aid's quality are considered. There are offered the parameters that can be calculated with the use of the data kept in medical information systems of treatment-and-prophylactic establishment. The usage of the offered model will allow making an initial estimation of the doctor's activity without calling medical experts. Due to this method the process of estimation will be more objective, fast and less expensive.

The medical attendance quality and its quality estimation criteria occupy a greater part of native scientists' attention [1-9]. The medical care quality estimation is indicative of the attitude of the state and society to health care problems.

In Russian public health service a paradox situation has formed in medical care quality estimation: drawing attention to a patient's social protection the health care provider's social protection has been completely forgotten. Nowadays the medical staff has no motivation to upgrading at all. The medical-diagnostic process quality should have positive material confirmation [5, 6]. The labour compensation in health care service should inspire the staff personnel to medical care refinement, resources conservation, take into account the complexity and intensity of their labour costs, i.e. be of stimulating character – this is the opinion which is popular not only among medical workers, but also among their patients [7].

Currently for a medical and prophylactic institution (MPI) the following official factors are used:

for hospital service:

- bed-day plan realization percentage;
- bed turnover;
- bed mean down time;
- hospital mortality percentage;
- mean time of hospital stay, etc.

for a clinical type MPI estimation:

- number of visits;
- load on one fill vacancy of a doctor in a polyclinic;
- percentage of visits because of a disease (prophylaxis);
- plan realization percentage on preventive examinations and prophylactic immunization.

Thus, the medical service delivery can be considered not to be estimated by the official factors.

The following medical care quality estimation factors are described in literature:

1.Factors for a MPI activity estimation according the final medical result [9], such as: infant mortality, morbidity with temporal disability (MTD), etc. On the ground of definite standard indicators an integrated work efficiency factor is settled. The achievement of every factor is measured in points taking into account its value. Then, on the basis of fulfillment of all planned factors the total "efficiency indicator" is defined.

2.The treatment level quality criterion (TLQ) [10]. The essence of the TLQ method is in comparison of really rendered medical assistance with the medical economical standard. A medical expert carries out the evaluation in accordance with specially developed scales.

3.The integrated efficiency coefficient [10] which is defined by means of medical, social coefficients and the coefficient of real and standard costs correlation.

These factors are used mainly for medical assistance estimation in hospitals. When using them the involvement of experts is obligatory. It makes the process of estimation more expensive and, besides, the human factor is present here that gives rise to bias.

With information technologies development the existing in MPI medical information systems (MIS) can be successfully used at solving problems of a doctor's activity estimation. Modern MIS represent an aggregate of not only softwear and hardwear tools, but a great amount of data bases and knowledge allowing automating different processes taking course in a MPI as well. With the help of MIS an integrated information space/noosphere for the information access acceleration is created, a health care institution activity transparency and, as a consequence, the efficiency of management decisions taken increases. On the ground of the data got from MIS it is possible to get a more or less objective estimation of medical activity using methods and algorithms worked up by different authors [8, 10].

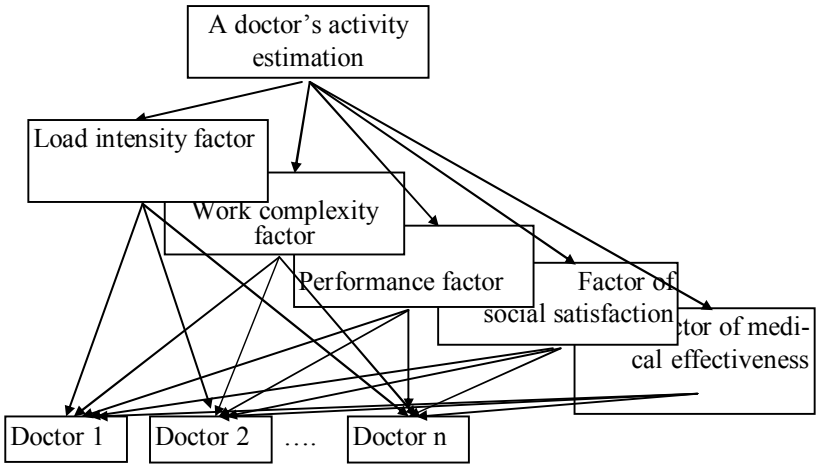
The most meaningful universal criteria of a doctor's labor activity estimation can be [8]:

- load intensity (volume of works);
- complexity of the performed work;
- quality of health care delivery;
- medical effectiveness;
- social satisfaction of the medical service consumer.

The quantity specification of a defined criterion is the corresponding factor and can be calculated on the basis of the data provided by medical information

systems. The aggregate of all factors can serve as an objective doctor's activity estimation. Naturally, the specific character of this or that MPI or its unit activity should be taken into account. In the given work we offer the criteria which were developed for the analysis of a specialized polyclinic establishment in which the data about all medical methods, rendered services, patients, etc. were cumulated in the MIS database over a period of years.

In terms of the abovementioned factors we obtained a hierarchic bilevel rating model of a medical activity estimation; it being represented in pic.1.



Picture.1. Hierarchic rating model of a doctor's activity estimation.

An integrated estimation of a doctor's activity can be obtained in terms of the following formula:

$$R_V = \nu_1 K^{Int} \cdot (\nu_2 K^{Sl} + \nu_3 K^{K} + \nu_4 K^{Mr} + \nu_5 K^{Su}) \quad (1)$$

where K^{Int} is the factor of load intensity;

K^{Sl} - the factor of the performed works complexity;

K^{K} - the factor of the performed works quality;

K^{Mr} - the medical effectiveness factor;

K^{Su} - the factor of social satisfaction of the medical service consumer; $\nu_1, \nu_2, \nu_3, \nu_4, \nu_5$ - values of weight factors determined by experts.

These values can be changed depending on the problems facing a medical and prophylactic institution in this or that period of time. Thus, a health care provider's activity control in the line of drawing his attention to some or other aspects can be exercised in a MPI.

As the factors can be measured in terms of different scales, it should be taken into account that the comparability of quantity indicators is possible only when their being standardized. Therefore, every criterion should be expressed by a ratio.

The factor of a doctor's load intensity K^{Int} serves for the estimation of the performed work amount of *i*-doctor and can be computed using the following formula:

$$K_i^{Int} = \frac{I_i^V}{\frac{1}{n}\sum_{i=1}^{n} I_i^V} \quad (2)$$

where I_i^V is the load intensity of the *i*-doctor and is defined as:

$$I_i^V = \frac{B}{T}, \quad (3)$$

B is the number of the patients treated within the analyzed period of time;

T - the actual time worked (hours) which is formed of T_1 - actual hours worked in the substantive posts; T_2 - the hours worked in the substitutive posts; T_3 - the percentage of combining the hours without working out the time (corresponds to the percentage for the enlarged service zone):

$$T = T_1 + T_2 + T_3, \quad (4)$$

The factor of the performed works complexity K^{Sl} can be computed in terms of the methods represented in the works of Shchepin O.P. with the colleagues [8]. At the heart of the methods there is a statement about the fact that the complexity of the works is connected with a doctor's labor intensity that, in its turn, is equivalent to the resource intensity of the medical diagnostic process. The tariff of the completed case medical economic standard reflects its resource intensity, inclusive of the medical activity intensity, and it means that it can be identified with the case complexity degree. Therefore, the completed case complexity factor K^{Sl} can be computed as a standard complexity factor of the *i*-doctor's performed work:

$$K_i^{Sl} = \frac{P_i}{\sum_{i=1}^{n} P_i} \quad (5)$$

where:

$P_i = \frac{\sum_{j=1}^{m} C_j^{MS}}{m}$ is the average cost of the completed cases of the *i*-doctor,

C_j^{MS} - medical economic standard *j* of that completed case;

m –the *i*-doctor's completed cases quantity;

n – the quantity of doctors as a whole.

Taking into account the fact that the current medical economic standards' tariff rates do not always correspond to either time and intellectual and physical labor costs of medical personnel, a completed case complexity factor can be estimated using expert corrections. The last are possible to develop in terms of an establishment work analysis for some previous years to cover a maximum possible number of different completed treatment cases for the generalizations' reliability. According to piling-up of materials the revision of the complexity factors estimations can be carried out.

For medical assistance quality estimation the factors are described in literature that can be divided into specific and universal ones. The specific factors are developed for every disease. This approach is considered to be rather expensive and requires a qualified expert available. The universal factors are closely connected with the health state of patients and indirectly estimate the quality of medical assistance rendered for a group of patients.

The quality estimation of rendering medical assistance is based in the whole on comparison of actually put into effect measures and the obtained results with the established "standards" or "models". Such notion as "quality standard" even exists [6]. The problem of correlation of notions "medical effectiveness" and "medical assistance quality" is rather complicated. Though the medical service quality is closely associated with the idea of medical effectiveness and lies in its foundation, these notions are not identical and, to the authors' opinion [8], it is necessary to use the factors reflecting both the result achievement degree and the characteristics of the process performed with this purpose. The factors of medical assistance quality estimation according the result, as the most objective and easy to obtain, are considered in the clause. Such estimations can serve as a method obtaining information for taking management decisions.

The factor of the performed works quality K^K.

The factor of medical assistance quality is equal to:

$$K^K = \beta_1 K^d + \beta_2 K^{sd} + \beta_3 K^{rem} + \beta_4 K^{-p}, \quad (6)$$

where K^d is the coefficient of health survey;

K^{sd} – the one of diagnosis coincidence;

K^{rem} – the remission coefficient;

K^p – the coefficient of repeated cases of visits to a doctor on one and the same nosology.

On the authors' opinion [6], the measures conducted by a doctor for a dispensary observation patient can accelerate the rehabilitation process and allow removing the patient from the dispensary list. However, if the doctor takes a decision about an unfounded removing the patient from the dispensary list, the disease progression risk will increase and the patient will have to seek for medical advice more often, that lead to his repeated including into the list or to the deterioration of another factor - the coefficient of repeated cases of visits to a doctor.

The coefficient of health survey for the i-doctor is defined

$$K_i^d = \frac{\frac{P_i^{Сд}}{P_i^{Пд}}}{1/n \sum_{i=1}^{n} \frac{P_i^{Сд}}{P_i^{Пд}}}, \quad (7)$$

where $P_i^{Сд}$ is the number of patients removed from the dispensary list for the period under review; $P_i^{Пд}$ – the number of patients included into the dispensary list for the period under review.

The coefficient of diagnosis coincidence is rather popular for medical assistance characteristics and described by many authors, but serves mainly for lethality cases characteristics. But we think that the given factor can serve for the estimation of a separate doctor activity as it allows evaluating the performed by the doctor diagnostic maneuvers which have allowed making a correct or incorrect diagnosis.

The coefficient of diagnosis coincidence for the i-doctor is equal to:

$$K_i^{sd} = \frac{\frac{N_i^{совп}}{N_i^{всего}}}{1/n \sum_{i=1}^{n} \frac{N_i^{совп}}{N_i^{всего}}}, \quad (8)$$

where $N^{совп}$ is the number of the given doctor diagnoses which have coincided with the diagnoses of the hospital with at the patient's admission to the day-and-night clinic with the MCC diagnosis, with an appointment card to the MCC, etc.;

$N^{всего}$ – the number of the diagnoses made for a time unit.

The remission coefficient shows the ratio of the time of sickness to the time of health and is one of the possible generalized characteristics of a patient's health [8]. At other equal conditions this factor can be closely connected with the doctor's work quality. A high level of corruption resistance can be expected from this factor as write-ups are impeded here, and if the doctor signed out a patient without completing the curing process, the patient soon can again seek for medical aid and the value of the considered factor will be deteriorated. Sure, the given factor depends not only on the quality of the rendered assistance, but also on a range of external causes (age, life mode of the patient and others), but it can be expected that owing to the law of large numbers random factors will become neuter, and the difference between the factors will be explained by the doctor's personality traits.

The remission coefficient shows how effective the performed treatment of the patients by the i-doctor is.

$$K_i^{rem} = \frac{1/m \sum_{i=1}^{m} \frac{T_i^{болезни}}{T_i^{здоровья}}}{1/n \sum_{j=1}^{n} \left(1/m \sum_{i=1}^{m} \frac{T_i^{болезни}}{T_i^{здоровья}} \right)} \quad (9)$$

where $T^{болезни}$ is the amount of time from the moment of visiting the doctor for the first time up to the termination of the treatment course (a completed case);

$T^{здоровья}$ – the amount of time after the termination of the treatment course up to the next visit to the doctor because of a sickness;

n – the number of the polyclinic doctors;

m – the number of the i-doctor's patients.

The coefficient of repeated cases of visits to a doctor on one and the same nosology shows how well the treatment was carried out and how seldom backsets occur.

$$K_i^p = \frac{\frac{N_i^{повт.сл.}}{N_i^{всего}}}{1/n \sum_{i=1}^{n} \frac{N_i^{повт.сл}}{N_i^{всего}}}, \quad (10)$$

where $N^{повт.сл}$ – is the number of repeated cases of visits during the year because of one and the same disease (is computed for the patients who are not in the dispensary list);

$N^{всего}$ – the number of completed cases for a given doctor for a time unit.

The weight numbers were offered by experts depending on what role this or that factor plays in medical assistance quality.

The medical effectiveness factor K^{Mr}

$$K_i^{Mr} = \frac{((K_i^r + K_i^l + K_i^g)/3)}{1/n \sum_{i=1}^{j} \left((K_i^r + K_i^l + K_i^g)/3\right)}, \quad (11)$$

where $K^r = \frac{N_{улучш}}{N}$ – is the coefficient showing the ratio of positive treatment results to the total quantity of patients;

$K^l = \sum_{n=1}^{m} \frac{T_n^{факт}}{T_n^{станд}}$ – the coefficient showing the ratio of the number of the hospitalized by a given doctor to the total number of the cured patients.

The factor of social satisfaction K^{Su} can be valued according to the results of patients' special interview:

$$K_i^{Su} = \frac{1}{\sum_{i=1}^{n} \frac{B_i^{удовл}}{B_i^{опр}}} * \frac{B_i^{удовл}}{B_i^{опр}} \quad (12)$$

where $B_i^{удовл}$ is the number of the signed out patients satisfied with the quality and culture of their i-doctor of a concrete department;

$B_i^{опр}$ - the number of the interviewed patients finished the treatment of the *i*-doctor of a given department.

For computing the offered factors using SQL-query the data from the medical information system of one of Surgut medical institutions were got. The database fields necessary for extracting information used further for computing the factors are represented in the table 1.

In table 2 the results of computing of nine factors of activity factors for 7 doctors according to the data of the medical information system of one of Surgut medical institutions of the polyclinic type are quoted. On the ground of the computed factors a generalized factor of a doctor's activity is quoted in the last heading.

For the composite index computation the importance weight coefficients of this or that factor, defined by experts, should be used. As the experts the leaders of the medical institution can act. In this very work the factors importance weight coefficients were recognized as equal against each other. On the ground of the computations a conclusion can be done, that the best results belong to Doctor 5, Doctor 6, Doctor 7 and Doctor 1.

Depending on the problems facing a medical institution in a concrete period of time the factors' importance can be changed. Thus, the leadership of a medical institution has got a management instrument permitting it to aim the efforts of the collective body at the performance of some or other problems.

Table 1. The necessary database fields for computing the factors

Factor		*Interpreted database fields*	*Extracted information*
Factor of load intensity	K_i^{Int}	Code of doctor Code of patient Date of visit Worked out time (number of wages)	Total number of completed cases Worked out time (including substantive posts, substituted posts, percentage of combination hours without working out the time).
Complexity factor	K^{Sl}	Code of doctor Code of patient Date of visit Sum to pay	Cost of completed case on j-nosology for i-doctor (actual) Integrated cost of doctor's work Integrated cost of work of all doctors
Factor of the performed works quality	K^d – health survey	Code of doctor Code of patient Date of visit Dispensary list (1- included, 2- signed in , 3- signed out)	Number of the signed in for a period of time Number of the signed out
	K^{sd} – diagnoses coincidence coefficient	Code of doctor Code of patient Date of visit Initial diagnosis Terminal diagnosis	Number of coincident initial and terminal diagnoses Number of visits
	K^{rem}– remission coefficient	Code of doctor Code of patient Date of visit	Duration of sickness (days), duration of health state (period of time from disease to disease)
	K^p– coefficient of repeated cases of visits	Code of doctor Code of patient Date of visit	Number of patients, having visited because of one and the same diagnosis for the second, third, etc. time for a period of time Total number of attendances for a period of time
Factor of medical effectiveness	K^r – coefficient of visit results	Code of doctor Code of patient Date of visit Result of visit	Number of positive results of completed case, total number of visits
	K^l – coefficient of treatment duration	Code of doctor Code of patient Date of visit Date of completed case termination Treatment duration according to standard	Ratio of treatment duration to standard treatment duration for completed cases
	K^g – coefficient of hospitalization	Code of doctor Code of patient Date of visit Result of visit	Number of patients admitted to a hospital, total number of treated patients
Factor of social satisfac-	K^{Su}		Number of patients satisfied with treatment quality of i-doctor to total number of interviewed patients of i-doctor

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Table 2. A doctor's activity factor

	Quality factor						Effectiveness factor			
	Intensity factor	Complexity factor	Coefficient of health survey	Coefficient of diagnoses coincidence	Remission coefficient	Coefficient of repeated cases of visit	Coefficient of visit results	Coefficient of hospitalization	Coefficient of treatment duration	Composite index of medical aid rendering quality estimation
Doctor 1	0,90	0,06	0,86	0,82	0,09	0,16	0,65	0,01	0,91	1,50
Doctor 2	0,86	0,08	0,90	0,75	0,01	0,22	0,58	0,01	0,99	1,28
Doctor 3	0,79	0,07	0,85	0,91	0,01	0,18	0,54	0,02	1,01	1,26
Doctor 4	0,72	0,18	0,92	0,84	0,01	0,19	0,64	0,03	0,89	1,24
Doctor 5	1,13	0,07	0,84	0,82	0,01	0,17	0,76	0,02	1,10	1,94
Doctor 6	0,94	0,10	0,90	0,82	0,22	0,16	0,70	0,04	0,99	1,77
Doctor 7	1,01	0,09	0,45	0,81	0,01	0,20	0,66	0,14	0,99	1,51

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CARBON DIOXIDE LASER USING EXPERIENCE IN HYPERTROPHIC SCARS TREATMENT

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Cicatrical defects on people's skin are ones of the most common pathologies in the world. On evidence of different authors up to 19% of all patients applied to medical institutions are with hypertrophic scars. Scar problem is of current interest as active working age young people suffer from them.

The purpose of the present work is to study a combined use of hypertrophic skin scars treatment by cryodestruction and CO_2-laser.

The method was used in 17 patients aged from 17 to 35 years old with hypertrophic skin scars from 1 to 5 years old. The patients with the scars were divided into groups according to the scar size. All the patients had linear form of scar. First, high-powered (15- 25 Watts) polishing with CO_2-laser of the most extruded scar portions in continuous beaming mode up to formation of thermal necrosis zone was performed. During the operation the power can be changed for some times. The marking is the tissue color local alteration, i.e. thermal necrosis in the center and the tissue blanching on the edge with ablative deformity. Then within the period from one to three days cryodestruction was carried out. The choice criterion was the termination of so-called "capillary whirl" circum the area of thermal necrosis. For cryodestruction exercise liquid nitrogen was applied. The manipulation is performed extremely quickly, in one movement, carefully taking the scar without touching the boundary zone which has a so-called "verge". Then germfree drapes with liberal amount of acerbine are overlapped.

At the cytological examination of touch smear it has been established that the healing process is accelerated on account of wound process course phologistic phase reduction. Cytologically: inflammatory-regenerative and regenerative cytogram type. It was manifested in quantity reduction of safe neutrophils up to 40-70 %, increase of tissular primitive polyphibroblasts, phibroblasts, lymphocytes up to 20-35 %, increase of macrophages number up to 5-10 %.

Bacteriological data testified to the decrease of the flora amount and the decrease of COI number by a factor of 2-3 in the wounds healed with acerbine.

In 9 persons the change of hypertrophic scars to atrophic ones was without dysfunction. These scars are easily disguised with usual dry powder. In two persons the result was poor positive, i.e. the scar is visually accessible but not skin surface overhanging, without tension function. One cryodestruction scar area elcosis case was marked. Because of allergic anamnesis the treatment with acerbine was carried out. Secondary adhesion with stellation scar formation was performed.

The given method can be recommended for linear skin scars elimination, it seems to be advisable to recommend acerbine using while cryo- and laser-burns owing to excellent cosmetic results, one of explanations of which the pH (acidity) coinciding with the pH of skin is; the method is possible to apply at keloid cicatrices.

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INFLUENCE OF ETHINYLESTRADIOL AND LEVONORGESTREL ON THROMBIN-FIBRINOGEN INTERACTION AND THROMBIN TOLERANCE (information II)

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Side effects [5, 12, 19] – hemostasis disorders and conjugated with it pathological states [1, 12, 19], are intrinsic to estrogen- and gestagen containing preparations applied in hormonal replacement therapy or contraception [3, 4]. It made clinicians pay attention to hemostasis while applying estrogen- or gestagen containing preparations [2]. Sex steroids accelerate lipid peroxidation (LPO) as well [22], that is attended by hypercoagulemia [16], and it heightened interest in investigation of LPO shifts under the influence of gestagens or estrogens in the context of hemostasis [8]. It is also important that hemorrhage affection is combined with deceleration, and thrombotism – with acceleration of thrombin-fibrinogen interaction (TFI) [5, 11], which inversely depends on thrombin tolerance (TT) and LPO activity [20].

Based on the above mentioned we experimentally studied plasmatic content of the TFI markers and TT changes at estrogen ethinyl estradiol (EE) and gestagen levonorgestrel (LNG) introduction in the context of LPO and AOP intensity in thrombocytes.

Methods: In experiments on white female rats (458 species, 170±15 g), fed with viscous consistency ration (barley and oat cereals mixture with oil), we studied the EE, LNG, prooxidant (lead acetate) and antioxidant – dimephosphon (DM), introduced with the morning portion of the ration, effects. Blood samples were taken from v. jugularis from fixed rats (narcosis – diethyl ether). The content of monomeric fibrin soluble complexes (MFSC) [18], fibrin degradation products (FDP) [15], D-dimers ("D-dimer test"-set of the firm Roche), P_3 and P_4 [10] factors, thrombin reacting fibrinogen concentration [14] and thrombin tolerance (TT) [13] were defined in the plasma. The content of diene conjugates (DC) was found out by optical density (λ - 232 nm) of heptanic phase; the content of lipid peroxides, reacting with thiobarbituric acid (TBA), was defined by fluorescence intensity (λ - 510 nm, fluorimeter "Bian130"). By the oxidation rate (OR) and induction period (IP) it was judged about the antioxidant potential (AOP) [21]. The results were evaluated by the method of variance analysis for small observational series, computing the average arithmetic (M), its average error (m), root-mean-square error (σ), confidence coefficient of Student (t) and the degree of difference possibility (p).

TFI and TT markers at EE introduction. The experiments of this family were carried out according to the scheme: the first group rats got the plain ration (control), the second one – the ration with EE (4 mcg/kg), the third – the ration with DM (1 g/kg), the fourth – the ration with DM (1 g/kg) and EE (4 mcg/kg). The samples were taken on the thirtieth day.

The EE introduction (table 1) increased the fibrinogen level and also those of FDP, FSC, D-dimers, P_3 and P_4 [10] factors, the content of DC, TBA, decreased the IP and increased the OR, i.e. accelerated the LPO rate and reduced the AOP. The DM introduction didn't influence the TFI markers, but reduced the LPO rate and increased the AOP. The DM and EE introduction eliminated the TFI shifts caused by EE. The content of DC and TBA turned out to be lower than in the control, the IP lengthened and the OR reduced. The thrombin tolerance decreased at the EE introduction and normalized at the introduction of EE+DM.

Table 1. TFI markers and thrombin tolerance in the rats fed with EE (4 mcg/kg), ДМ (1 g/kg) or EE+DM for 30 days

Factors	Experiment groups (n = 10 in a group)			
	Control (plain)	EE introduction	DM introduction	EE+DM introduction
FG, g/l	2.6±0,22	3.4±0,11*	2,4±0.22	3,3±0,24*
FDP, mg%	15,3±1,1	20,1±1,2*	14,8±0,8	16,5±1,7
MFSC, mcg/ml	22.0±0.9	26.9±0.8*	21.9±1.2	23.9±1.9+
D-D, ng/ml	0.18±0.03	0.26±0.04 *	0.17±0.03	0.17±0.04+
F. P_3,%	82,5±1,0	89,9±1,3*	79,7±1,3	84.0±1,3+
F.P_4, c	2.3±0,01	3,1±0,03*	2,2±0,04	2.4±0,01+
DC, A/mg of a lipid	0,082±0,002	0,094±0,003*	0,075±0.002*	0,078±0,002+
TBA, unit/mg of a lipid	0,21±0,005	0,32±0,002*	0,17±0,004*	0,22±0,003+
IP, min/ml	45.1±1.8	37.5±1.1*	52.7±2.1	47.5±1.3+
OR, mm3/ml/min	0.74±0.02	0.80±0.03*	0.62±0.03	0.73±0.03+
TT, %	100±4.9	61.2±3.4*	105±3.4	98.7±4.5

Symbols and notations: FG – fibrinogen, FDP – fibrin degradation products, MFSC - monomeric fibrin soluble complexes, D-D – D-dimers, F. – factor, DC - diene conjugates, TBA – products reacting with TBA, IP – induction period, A – optic density, OR – oxidation rate, DM – dimephosphon, TT – thrombin tolerance; * sign – authentic differences when compared to the first, + - to the second column.

In the second series of the experiments (the scheme is the same) the samples were taken on the 10^{th}, 20^{th} and 30^{th} day and it was found out the following: at EE introduction, especially with lead, the LPO shifts are more noticeable; at EE, lead and DM introduction there are no shifts, i.e. the lower LPO and higher AOP – the higher TT; the lower AOP – the lower TT. Probably, the TT (which characterizes animals' ability to stand hyperthrombinemia) decreases at the LPO acceleration revealed simultaneously with the growth of the TFI markers level and increases at the AOP increase, i.e. at the TFI markers level decrease.

Intensity of TFI, LPO, AOP and TT at LNG introduction. The LNG dose (6.4 mcg/kg) is higher than that of EE as well as the content of LNG in preparations for combined oral contraception. The scheme of the experiments is the same.

Signs and notations: as in table 1.

From the data of table 2 it is seen that at LNG introduction the TFI, fibrinogen, LPO, AOP and TT markers level shifts are similar, but less signified than at EE introduction. At simultaneous introduction of LNG and DM hemostatic shifts there are no changes of the LPO, AOP and TT occurred.

While studying the dynamics of the caused by LNG shifts occurrence, we carried out an experiment analogous to the one with EE. It appeared that the LPO acceleration and growth of the TFI markers level at the LNG introduction, especially with a prooxidant (lead), are more vivid; at simultaneous introduction of LNG, prooxidant and DM shifts never appeared. As in the experiments with EE the TFI markers level changes and LPO acceleration appear simultaneously, and the TT shifts are opposite on the directivity to the LPO shifts.

Table 2. TFI markers and TT in rats fed with LNG (6.4 mcg/kg), DM or LNG+DM for 30 days

Factors	Experiment groups (n = 10 in a group)			
	Control (plain), n - 9	LNG introduction, n -10	DM introduction n -10	LNG+DM introduction, n -10
FG, g/l	2.5±0,21	3.2±0,10*	2,5±0.23+	2,9±0,12*+
FDP, mg%	15,8±0,8	18,1±0,9*	14,8±0,8+	16,0±1,0+
MFSC, mcg/ml	22.3±0.8	25.1±0.7*	21.1±1.1+	23.3±.9+
D-D, ng/ml	0.17±0.02	0.21±0.02*	0.18±0.02+	0.17±0.03+
Ф. P_3,%	81,1±1,0	85,9±1,0*	79,9±1,1+	82.1±1,1+
F.P_4, c	2.4±0,02	2,8±0,02*	2,3±0,03+	2.4±0,02+
DC, A/mg of a lipid	0,085±0,003	0,093±0,002*	0,076±0.002*	0,077±0,003+
TBA, unit/ mg of a lipid	0,23±0,004	0,30±0,002*	0,18±0,003*+	0,23±0,004+
IP, min/ml	44.8±1.6	38.9±1.0*	52.1±1.8*+	47.9±1.2+
OR, m3/ml/min	0.76±0.03	0.83±0.03*	0.64±0.02*+	0.74±0.04+
TT, %	100±3.9	72.2±3.7*	104±5.4	99.5±4.5

Further it was testified that with the EE or LNG dose increase 2, 3 and 4-fold the TFI, LPO, and AOP markers level shifts surplus is not in proportion to the dose – the increase of the dose 2, 3 and 4-fold

intensifies the shifts only 1.2, 2.4 and 3.0-fold accordingly. At simultaneous EE and LNG introduction in all tested doses the TFI markers level shifts and LPO rate summarized incompletely, with the dosage increase the summation degree reduced.

Conclusions

1. At oral introduction in the dosage equivalent to antiovulatory dose for a human being EE lowers the AOP, accelerates the LPO and TFI and reduces the TT. The effects intensify with the introduction duration increase.

2. Oral introduction of LNG in equivalent doses causes less signified LPO, AOP, TFI and TT shifts of the same directivity intensifying with the introduction duration increase. **3.** At combined introduction of EE and LNG their effects on the TFI, LPO and AOP summarize only partially. **4.** An antioxidant (DM) introduction simultaneously with EE or LNG eliminates their effects on the LPO, AOP and TFI. **5.** Between the AOP of thrombocytes and TT there is a close, and between the LPO acceleration degree and TT – inverse, relationship.

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ANTIBIOGRAM ANALYSIS IN PATIENTS WITH II-III DEGREE BURNS

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Antibiotic therapy takes a leading place in complex treatment of patients with II-III degree burns S complicated with pyoinflammatory processes of soft tissues. Nowadays growth of causative agents' multiresistant strains to germicides in the given patient group is registered. That is why the disease differs from others with long-term and persistent treatment course, appreciation of treatment.

Purpose: To investigate the etiological structure of the causative agents and the spectrum of their sensibility to germicides at burn disease.

Materials and methods: In the paper the bacteB riological research analysis of the material from the burnt surfaces of 199 patients and autogenerated causative agents' sensibility to 29 germicides with the disco-diffuse method using.

Results: The contamination of the material under examination made 96,5%. The dominant activators of the burnt infection were S.aureus (50,8%) and Ps.aeruginosa (20%). From opportunistic enterobacteria Proteus (6,7%), E.coli (5,6%), Enterobacter (5,1%), Klebsiella spp. (2,6%) were plated most commonly. In 50,2% of cases combined infection forms consisting of two and more kinds, being formed on account of tolerant associations, were marked: S.aureus and Ps.aeruginosa (51,0%), S.aureus and enterobacteria of different kinds (31,0%). The antibiogram studies demonstrated nonsensibility of S.aureus to penicillins (0,9%). The most effective preparations against the given activator were: ofloxacin (45,7%),

ciprofloxacin (32,4%), carbapenems (45,7%), rifampicin (44,8%), fusidic acid (32,4%), gentamicin (22,9%). From the cephalosporin group S. aureus was sensible to ceftriaxone in 28,6% of cases and to cefazolin in 24,8% of cases, and to the representatives of the third generation – to cefoperazone (9,2%) and ceftazidine (10,5%). Antipseudomonal activity was manifested in carbapenems (53,8%) and monofluorchinolones (ofloxacin - 43,6% and ciprofloxacin - 41,0%). From the aminoglycoside group the activator was more sensible to amikacin (20,5%), than to gentamicin (15,4%). Only ceftazidim from the cephalosporin series was active in regard to Ps.aeruginosa in 25,6% of cases. The bacteriostatic effect to S. aureus and Ps.aeruginosa occurred on the part of semisynthetic tetracyclines in doxycycline (13,3% and 25,6% accordingly). The increase of enterobacteria was suppressed in the majority of cases by: ceftriaxone (41%), ceftazidime (35,9%), imipenem (46,2%), gentamicin (43,6%), ciprofloxacim (41,0%), piperacillin (28,2%), chloramphenicol (20,5 %).

Conclusion: Antibacterial therapy of burn disease infectious complications is determined by the spectrum of probable activators. Monofluorchinolones and carbapenems turned out to be the most effective antimicrobial agents as the result of the research.

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THE CYTOKINE PROFILE IN THE ACUTE CRYOTRAUMA

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Nowadays cold trauma is considered to be one of the most important causes resulting in high rate of disability or death among patients. The most frequent manifestation of cold trauma is frostbite occurring both in high and low latitudes. One may sustain cryotrauma even at warm weather.

The main aims this study are to estimate the adaptive mechanisms of the organism in developing cold trauma and investigate interleukin1 β (IL-1 β) and the factor of tumour necrosis α (TNF α) under the influence of potent irritant.

Materials and methods: the experiments were carried out on the male mature Vistar rats with the body weight 200-240gr. The models of frostbite induced by chlorethyl were employed within one week after damage. The withdrawal of rats was implicated by means of decapitation under etheric anesthesia in an hour, 24 hours, on fifth and seventh days. The approval of Ethics Board of the Northern state medical university was obtained. «The Regulations of the work with experimental animals » were observed according to the Enactment of Ministry of Health of the USSR №755 issued 12.08.1977.

The contents of the anti-inflammatory cytokine IL-1 β and TNF α was determined in blood serum with the help of immunofermental method using reagents manufactured by "RD Systems", USA. Experimental group was affected by cold. Control group consisted of intact animals. Statistical analysis was done on the basis of Statagraphcs plus 5.1 for Windows.

Results: the study demonstrated that the production of cytokine was dramatically decreased in the early reactive period (in one hour and 24 hours after damage) and sharply increased at the beginning of the late reactive period (at $p \leq 0{,}001$). The imbalance of anti-inflammatory cytokine was observed at all experimental stages the secretion of TNF α prevailed. We suggested that in intact animals revealed cytokine performed a certain "sentry" function since it was this cytokine that was the mediator of « the first wave » responsible for triggering defensive immune mechanisms.

Conclusions: the secretion of cytokine IL-1 β and TNF α in a healthy organism reflects the current condition of immune system. Imbalance of cytokine at frostbite specifies indicates their role in pathogenesis of acute cryotrauma and may be of a certain value in diagnostics of the severity of injury in the monitoring cryotrauma and in developing new methods of treatment, which may prove to be more effective, than traditional ones.

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INVESTIGATION OF MEDICINAL TEAS APPLIED IN HYPOFERRIC ANEMIA PHYTOTHERAPY

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Drug therapy of hypoferris anemia is based on the introduction of iron from iron containing medicinal agents into the body. The substitution therapy of iron deficiency by means of its salt preparations is effective enough, however, a serious adverse events development risk, even while using modern synthetic medicinal agents, remains rather high. At the same time, phytotherapy as one of the treatment modes is deprived of disadvantages natural for drug treatment with using xenobiotic medications of synthetic origin. Phytotherapy is recommended as a means of complementary therapy and especially effective for iron deficiency prevention at hidden iron deficiency.

With that, it is necessary to note that monotherapeutic approach based on using only one from almost 200 plants used in folk medicine doesn't allow combining etiotropic and nosotropic disease therapy. An optimal phytocomposition for anemia therapy should contain trace substances of blood-forming complex in addition to the complex of organic nature bioactive compounds (Fe, Mn, Cu, Co). To create a phytomixture of a necessary composition is possible only using several medicinal plants in the form of tea. Medicinal plant tea allows providing the required polyvalency of the pharmacological action phytopreparation.

In connection with the above mentioned to investigate the elementary composition of total abstractions from the teas most often recommended in science and folk medicine for phytotherapy appears to be of current interest. As the subjects for inquiry (table 1) the most often used in folk medicine medicinal plant teas and also the tea with a well-antianemic activity (№3) were used.

The collected medicinal plant raw material (MPR) was brought into the air-dry condition. Special medical plants were granulated as large as 1,0 mm particles. The teas were made by mixing the granulated MPR in the required for every tea proportion up to homogeneous condition. For obtaining the total abstraction an accurate batch weight of the raw material (a separate plant or their mixture as the tea ingredients) was put into a bulb. Then the raw material was poured with an extraction agent in the ratio 1:50. Distilled water was used as the extraction agent. The extraction was carried out for 2 hours on boiling water bath in a bulb with an under reflux. In the closing stage the abstraction percolation was performed and the aliquot for the micro-elementary analysis was taken away from the infiltration.

The trace element content of the blood-forming complex (being an essential component of blood-forming) - Fe, Mn, Cu and Co was defined by the method of mass-spectroscopy with inductively coupled plasma. The reproductibility of measurements was 3,0; 3,0; 10,0 and 4,0% at Mn, Fe, Co, and Cu concentration determining accordingly.

Table 1. Trace element content in total abstractions from MPR (mg/l).

№ and ingredients of the tea	Fe	Mn	Cu	Co
1. *Betula pendula, Mentha piperita,Juglans regia*- folia; *Hipericum perforatum, Onopordum acanthium, Cichorium intybus, Lamium alba* – herba; *Juniperus communis* - fructus	0,199	2,230	0,054	0,001
2. *Hipericum perforatum. , Lamium alba, Achillea millifolium*– herba; *Fragaria vesca*- folia; *Avena sativa, Vaccinium myrtillus* – cormi; *Glycyrrhiza glabra* - rizomata -	0,141	1,600	0,077	0,0004
3. *Bidens tripartita, Fragaria vesca, Urtica dioica* – folia; *Rosa majalis* - fructus	0,449	0,460	0,072	0,002
4. *Betula pendula, Fragaria vesca, Urtica dioica,Ribea nigrum* – folia; *Rosa majalis* - fructus	0,263	2,700	0,054	0,005
5. *Betula pendula, Fragaria vesca, Urtica dioica,Ribea nigrum, Rubus caesius*– folia; *Pulmonaria obscura, Agropyron repens* – herba; *Avena sativa* – cormi;	0,196	1,420	0,049	0,002

The micro-elementary composition of the total abstractions (table 1) testifies that for the abstractions from the tea №3 the iron and manganese contents are equal and it is this very tea that proves the antianemic activity on nosotropic mechanism of action (iron rebalancing in the body). In this connection it is necessary to note that the quotient of the standard oxidation potentials Fe^{3+}/Fe^{2+} and Mn^{3+}/Mn^{2+} guarantees "in vivo" unprompted reaction of oxidation Fe^{2+} into Fe^{3+}, in which the pair Mn^{3+}/Mn^{2+} will play the role of an oxidant. The ferric iron is deprived of the side effects natural for Fe^{2+} (citotoxicity). At the same time, finding ions Fe^{3+} in chelate polysaccharide complexes can prevent the carry-down of slightly soluble salts of Fe^{3+}. The required content of the polysaccharides in the phytocomposition provides the tickseed herb (*B.tripartita*). In its turn, the entry of such a polysaccharide complex of Fe^{3+} into the body most probably will lead to activation of triad ions carrier proteins – mobilferrin and b3-integrin, that activates the iron utilization from the coming food and by this will guarantee the iron rebalancing in the body.

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SOME ASPECTS OF VISCEROCARDIAL INTERACTIONS AT CORONARY HEART DISEASE

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Purpose of the work is to estimate the nosotropic significance of the abnormal gastroesophageal reflux on the ground of a clinical-instrumental examination of electrical instability markers of the cardiac muscle and viscerocardial interactions in coronary heart disease (CHD) patients.

Materials and methods. 225 patients were examined: 67 patients with a combination of CHD and gastroesophageal reflux disease (GERD) – the main group, and two groups of comparison: 72 CHD patients and 86 GERD ones.

According to sex-age composition the patients were commeasured: in the group of patients with the combined nosology the average age made 59±11,4 years old, there were 33 (49,3%) women there; in the patients' group with CHD the average age made 59±11,0 years old, 34 (47,2%) women; in the group of patients with GERD the average age made 56±10,6years old, 40 (46,5%) women.

The inclusion criteria: CHD (unstable angina, exertional angina of II-IV functional class, old myocardial infarction in the anamnesis), endoscopically positive GERD.

The exclusion criteria: clear rhythm or capacity disorders (atrial fibrillation, paroxysmal forms of tachyarrhythmia, frequent extrasystole, pulse generator availability, etc.), acute myocardial infarction during last two months and noncoronarogenic forms of the cardiac muscle damage, cardiac failures, signs of progression of acute or a chronic infectious disease recrudescence, cardiac decompensation of IV functional class according to NYHA, malignant neoplasms, endoscopically negative GERD.

The CHD was verified by the presence of old cardiac infarction or typical clinical presentation together with a positive take of stress-test (cycle ergometry), or together with the acknowledged episodes of myocardial ischemia at days ECG monitoring (SM ECG).

The diagnostics of endoscopically positive GERD was mediated by fibroesogastroduodenoscopy (FEGDS). The esophagus inflammatory-destructive processes' depth was carried out at total morphological investigation of biopsy materials of esophageal mucosa, the GERD with reflux esophagitis (RE) catarrhal and erosive forms was found.

As myocardium electrical instability markers the duration and asynchronism of repolarization processes, heart rate variability factors (HRV) were defined. In the standard ECG tested in generally accepted derivations the QT interval duration, QT interval dispersion (QTd) and QT corrected interval (QTc), which was computed using the formula of H.Bazett modified by L.Taran и N.Szilagyi, were calculated. The SM ECG was carried out with the help of Cardiotechniques-4000 system; standard factors of HRV were taken into account: high frequency waves capacity within the limits of 0,4 – 0,15 Hz, Рдв (HF), low frequency waves capacity within the limits of 0,15 – 0,04 Hz, Рмв1 (LF), average value of NN-intervals' standard deviations calculated on 5-minutes periods during the whole record (SDNNi), the initial value of the most commonly occurring R-R intervals (MODA), relative high frequency waves' capacity value expressed in normalized units (HF in n.u.), relative low frequency waves' capacity value expressed in normalized units (LF in n.u.), total power of the spectrum (TP), percentage of the sequential intervals' diversity more than 50 mc (PNN50).

The statistic analysis of the findings was carried out with the help of standard statistic packages of programs Statgraphics, 6,0 version Statistica.

Results. A range of myocardium electrical instability markers' state features was found out, thus, CHD patients authentically ($p<0,05$) differed from GERD patients with normal QT, QTc and QTd excess incidence; in the CHD patients a more significant asynchronity of repolarization processes compared to the GERD patients was found authentically ($p<0,05$). At comparison of the showings of the patients with CHD and GERD combination and patients with "isolated" CHD it is found that the average QTc, QTd in the group of patients with the combined pathology were authentically ($p<0,05$) higher than in the patients with CHD. The investigation of features of repolarization processes depending on the degree of RE testified that in the group of patients with the combined pathology an authentic increase ($p<0,05$) of the duration and repolarization processes asynchronity with an erosive variant of GERD unlike the patients with catarrhal RE is registered.

At the analysis of HRV factors authentically lower ($p<0,05$) values of HF, LF, MODA, TP, SDNNi and PNN50 compared to the group of patients with "isolated" CHD have been detected in the patients of the main group. The combined pathology patients authentically differed ($p<0,05$) from the GERD patients on all investigated factors of HRV. The HRV factors comparison in the group of patients with the combination of CHD and GERD depending on the degree of RE allows speaking on an authentic decrease ($p<0,05$) of HF, LF, HF in n.u., LF in n.u., MODA and TP with erosive changes of the lower third of the esophagus. No similar tendency was detected in the GERD patients group.

A multivariate regression analysis of the findings was carried out, and it testified that the intensity of RE exerts an independent authentic ($p<0,05$) influence on both myocardium inhomogeneity (QTd) and HRV factors.

Conclusions. The characteristics of coronary heart disease in the aspect of transnosologic co-morbidity with gastroesophageal reflux disease are: 1. the decrease of the cardiovascular system adaptative capacities, lower stress tolerance of the body and greater probability of the myocardium electrical instability; 2. the depth of the esophagus structural changes – the independent factor of the myocardium electrical instability risk in the given class of patients.

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PROTRACTED FORMS OF BETA-BLOCKERS AT COMBINATION OF CORONARY HEART DISEASE AND GASTROESOPHAGEAL DISEASE

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Transnosologic co-morbidity is one of the most complicated problems practitioners come across at drug treatment prescriptions. The combination of coronary heart disease (CHD) and gastroesophageal reflux disease (GERD) is a common clinical situation. It is found out that the gastroesophageal area damage occurs in 35 % of cases in the CHD patients. The pathogenetic therapy of CHD including beta-blockers leads to blood pressure decrease in the lower esophageal sphincter (LES) and increase of the episodes of its transitory relaxations; that, in its turn, becomes one of the risk factors for GERD progression. Whereas we found that the gastroesophageal reflux (GER) and the reflux esophagitis (RE) are the independent risk factors of the myocardium electrical instability in the patients with CHD and GERD combination. Thus, the problem of searching means for the CHD therapy, that do not influence the NPS tonus in patients with CHD and GERD synthropy (that will improve the prognostication in the given class of patients), is extremely pressing. We have supposed that the features of pharmacokinetics of unprotracted and retarding forms of medicinal preparations, which are connected with the intensity of variations of the preparation concentration in blood, can turn out to be significant.

We have carried out an open randomized study of metoprolol tartrate's protracted form safety (Metocard® Retard, production of «Polpharma», Poland) and metoprolol tartrate's unprotracted form safety (Metocard®, production of «Polpharma», Poland) in patients with CHD and GERD association.

Materials and methods. 60 patients were examined. They were randomized into 2 groups of 30 persons in each one. The inclusion criteria: CHD. Exertional angina of 2-3 functional class and /or CHD. Old myocardial infarction combined with endoscopically positive form of GERD, acceptability of beta-blockers. The GERD was diagnosed on the data of fibroesophagogastroduodenoscopy (FEGDS). The exclusion criteria: acute forms of CHD, noncoronarogenic forms of the cardiac muscle damage, acute infectious diseases, chronic illnesses in decompensation stage, cardiac failures, cardiac decompensation of IV functional class according to NYHA, malignant neoplasms, well-known contraindications to metoprolol application. The patients of both groups were commeasured according to their sex, age (the average age - 65±5) and comorbidity. The investigation duration was 30 days. The first group patients got 200 mg of Metocard® Retard per day; the second group got Metocard® in daily dose of 200 mg. Besides the specified preparations all the patients got ACE inhibitors, antiaggregants and inhibitors of protonic pomp in standard doses. For the purpose of estimation of the total GER episode number per day and daily average factor of intraesophageal pH (IP pH) the daily IP pH-monitoring with the application of "Gastroscan-24" unit was used, and it was carried out right after the randomizing and in 30 days from the starting moment of the investigation.

Results. The initial examination data in the selected groups didn't differ. At the administration of the protracted preparation the IP pH-metria factors authentically didn't change, while in the patients, who got unprotracted metoprolol, the last some deteriorated. In the patients, who got Metocard®, the daily average IP pH factor after the treatment made 3,31±0,12, while in the patients, who got Metocard® Retard, - 3,61±0,11 (<0,05). At the investigation of the total number of GER episodes per day authentic differences (<0,05) were obtained: the minimal number of GER episodes was registered in the patients, who got Metocard® Retard, and the maximal one – in the patients, who got Metocard®. Thus, according to the data of IP pH-metria, the GER intensity was authentically more (<0,05) in the patients, who got the treatment with Metocard®, than in the patients, who got Metocard® Retard.

Conclusions. The findings allow supposing a more unfavourable run of GERD, and accordingly, a more risk of myocardium electrical instability development in patients with combined pathology at unprotracted metoprolol form application. Thus, Metocard® Retard is the agent of choice in patients with coronary heart disease synthropy and gastroesophageal reflux disease.

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EVALUATION OF HAEMODYNAMIC STATE IN EARLY STAGES OF ARTERIAL HYPERTENSION IN YOUNG MEN

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Arterial hypertension (AH) in the Russian Federation, as well as in all countries with advanced economy, is one of the burning medico-social problems. A considerable increase of AH patient census among non-adults frightens, while the diagnostics of the arterial tension (AT) increase in young people and the level of AH early stages detection stay unsatisfactory. From this perspective the most applicable methods are the ones of functional diagnostics, which allow detecting the states on the edge of the norm and pathology, early and super early changes on the part of the blood circulatory system for the purpose of probable cardiovascular diseases prognostication. To the advanced noninvasive methods of haemodynamics diagnostics the polyrheocardiography method integrating the research of central haemodinamics according to Kubichek and rheography of the pulmonary artery and aorta is referred.

The purpose of the present study was in the evaluation of haemodinamic changes of the systemic and pulmonary circulations in arterial hypertension early stages in young men by the computer polyrheocardiography method.

For the investigation of the systemic and pulmonary circulations haemodinamics state 38 men aged from 18 to 50 (the average age 35,1 ± 3,2) were examined. At the AH classification the Russian recommendations worked out by the Committee of Experts of the All-Russia Scientific Society of Cardiologists in 2004 were used. The first group consisted of 12 men with high normal AT, the second one – 13 patients with the AH of the first stage, and the control group made 13 practically healthy men matching in age. Coronary heart disease, backward heart failure, secondary hypertension and endocrinopathy patients were excluded from the examination.

For the purpose of the systemic and pulmonary circulations haemodynamics state determining the method of polyrheocardiography was used with the help of the"Rheo-Spectrum" multifunctional computer rheograph of the Russian firm "NeuroSoft". The statistical treatment of the materials was carried out by methods of descriptive statistics using the application program package "Statistica 6.0" and nonparametric techniques of valuation.

As a result of the carried out central haemodynamics investigation in both study groups the increase of the average haemodinamic pressure of different manifestation degree against normosistolia has been detected: at the high normal AT – by 9% and at the AH of the first stage – by 15% compared to the control group. In all patients including the control group the hypokinetic type of central haemodynamics was detected. The central haemodinamics state peculiarity in AH patients became the increase of vascular resistance: in the first group the total peripheral resistance (TPR) is increased by 39% and in the second group – by 7% compared to the control group, that testifies to the increase of the left ventricle afterload in the early AH stages. The cardiac output decrease in AH patients compared to the control group didn't exceed 2%. With the AT degree increase in the study groups the left ventricle preload decreased as evidenced by the left ventricle end diastolic pressure decrease. The TPR increase leads to the left ventricle contractive activity increase: in the group with high normal AT the Blumberger's coefficient was increased by 40% and at the first stage AH – by 81%. The detected changes of the systemic blood flow in the pulmonary circulation in the second group patients were characterized by hypertonia of small and medium arteriae, hypotonia of veins and they were manifested with the increase of slow blood filling time by 7% and the decrease of the rheographic diastolic index by 21% compared to the control group. The pulmonary hypertension has been detected in both groups of study, but the most frank it is in the patients with high normal AT.

Thus, early haemodynamic changes in both blood circulations have been detected by the polyrheocardiography method in young men in early stages of AH. The pulmonary hypertension progression preceding the left ventricle failure development is registered; diastolic dysfunction forthcoming against this background is the following reason for tension rise within the pulmonary artery system on account of the bulk factor including and vascular pulmonary resistance intensity.

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TRACE SUBSTANCES OF ANTIPARASITIC MEDICAL PLANTS

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In spite of medical substances organic synthesis success the vegetational resources still remain one of the basic sources of medical substances obtaining. The Kuzbass flora has great resources of medical plants with antiparasitic properties. A considerable increase of the contaminated with helminthoses people served the primary factor predisposing to Kuzbass antiparasitic action medical plants trace substances composition studies. Of all the examined on helminthoses – enterobiasis makes 68%, ascariasis – 19%,

opisthorchiasis – 12% and 1% falls at other less common parasitoses.

The role of inorganic plant elements is many-sided: they are parts of cellular structures, take part in biochemical processes, determine the conformation of organic molecules and membrane permeability, influence the living body signaling system functioning, and the main thing is that they take part in the processes of biosynthesis of plant active agents which are necessary for their medical properties manifestation. According to one of the classifications chemical elements are subdivided on the grounds of their importance for the plants: 1) essential macroelements (magnesium, calcium, potassium, nitrogen, phosphorus, sulphur) and microelements (manganese, molybdenum, nickel, cuprum, ferrum); 2) useful elements (sodium, cobalt, chrome, selenium, aluminon). We succeeded to find out all the numerated above substances in Kuzbass antiparasitic action medical plants: absinthium, mugwort, ginger plant, sown garlic, field pumpkin, bulb onion, wild carrot, poisonberry, common hop, garden huckleberry, horseradish, horseheal. Anthelminthic properties of these plants are assured by mineral substances partaking in the synthesis of alkaloids, flavonoids, glycosides, terpenoids. At the same, time geochemical factors and infestation with phytohelminths, which stimulate the accumulation of a range of elements (molybdenum, selenium, chrome, ferrum) in host-plant tissues, influence the content of mineral elements in the plants. These elements shortage in the soil promotes the plants protective properties reduction intensifying pathological processes in their nature at the phytohelminths infestation.

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FASTING-DIET THERAPY INFLUENCE ON SALT GUSTATION THRESHOLD

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Arterial hypertension (AH) is the most common disease concerning cardiovascular pathology. Its connection with heavy consumption of sodium salt is evident. The carried out research (Volkov V.S. and co-authors, 2004) testify the existence of high salt gustation threshold (HSGT) in arterial hypertension teenagers. However, more than a half of the teenagers with AH are overweighted. In this context the HSGT level in teenagers with AH in combination with overweight with Quetelet index more than 25 and fasting-diet therapy influence on HSGT.

56 teenagers with AH combined with overweight were examined. The average age was 14 years old (± 2,6). Besides general clinical-laboratory research the HSGT was studied according to the modified method of Henkin R. (Konstantinov Ye.N. and co-authors, 1983). In accord to the HSGT level the examined patients were divided into three groups: 4 (8,4%) teens had the HSGT level below normal one, 2 (4,2%) – had a medium HSGT level and 50 (87,4%) teens had a higher level of HSGT.

We also raised a question of the HSGT disturbance remoteness. On this basis the examination of 150 teens aged from 14 to 17 was carried out. The analysis of the findings testified that 130 (86,7%) teens have a higher level of HSGT. In the given group the HSGT study in 36 children with periodical arterial pressure rise against the background of overweight. The research data found out the HSGT increase both in the teenagers and their mothers.

A fasting-diet therapy in agreement with the guideline of the USSR MHC (1990) was carried out. The cycle lasted 19 days. Due to curative measures the HSGT decrease was registered in 50 (89,3%) of 56 teenagers. Not only the dynamics of arterial pressure decrease in all the patients was noticed, but also body weight losing by 6,4 kg.

So, it is detected that the HSGT level increase in teenagers has a burdened heredity. the carried out fasting-diet therapy has not only a positive effect at AH and decreases body weight, but also promotes the salt gustation threshold decrease.

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PATHOLOGIC ANATOMY AND MOLECULAR BIOLOGY ON THE BOUNDARY OF MILLENIA

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The role of pathoanatomy in the development of biomedical sciences is of great value and diversity. A wide introduction of biochemical methods, and in morphology – histological chemistry, allowed studying metabolic and molecular changes. The progress of molecular biology and immunohistochemistry, in situ hybridization became the foundation for creation of a new discipline – molecular pathology studying molecular biology of general pathologic processes and diseases in the level of structure, functional activity and gene expression changes.

The pathoanatomy gradually co-opted current achievements and up-dated engineering solutions of such sciences as anatomy, physiology, chemistry, microbiology, immunology, genetics, cellular and molecular biology. Nowadays it has got an opportunity to

study structural and functional imperfections starting with the organismic level and finishing with the molecular-genetic one.

Let us define the main engineering achievements of medical and biological sciences which have given the master pulse to the development of modern pathoanatomy, which nowadays combines elements of classical and molecular pathology, in brief.

The methods based on the immune mechanisms rest on the interaction of human tissue and molecular antigens with specially obtained antibodies bearing various marks on themselves. The light imuunohistochemistry antibody marks can be represented by various fluorochromes, horseradish peroxidase, alkaline phosphatase, peroxidase-antiperoxidase, avidin-biotin-peroxidase and avidin-streptavidin-peroxidase complexes, and also radiogenic substances. In the electronic immunohistochemistry it is preferable to use the marks in the form of colloid silver or gold.

The light immunohistochemistry allows revealing antigens in tissue and cellar levels and evaluating the resultant amount on the fluorescence intensity or tissue coloration. The electronic immunohistochemistry is used to study the subcellular antigen focalization.

The immunohistochemistry serves also for the evaluation of cell-specific gene expression on the corresponding protein products, coded by the given genes, in tissues and cells.

The immunohistochemical cells' marks coupled with their flow cytophotometry, laser and computer sorting allow detaching cell groups according the availability of definite antigenic determinants that is widely used in the hemopathy diagnosis.

The investigation of disease molecular foundations is associated with the identification of separate products (abnormal proteins, for example), transmission paths of cellular and intercellular signals, and synthesis of definite proteins, glycol- and lipoproteins.

The development of modern DNA analysis became possible after the discovery of series of enzymes (endonucleases, restrictases, polymerases, transcriptases) providing specific manipulations with DNA and RNA. Due to the fact it became possible to obtain specific fragments of the DNA molecule from different cells and tissues, to synthesize amino acid sequences typical of definite proteins, to create new DNA molecules by the recombination of molecule fragments from different sources. The newly synthesized DNA molecules' fragments are often used as a cloning vector for separate proteins with predetermined properties. The fragments of already existing DNA are transformed with the help of endonucleases to the vectors which are distributed in phages in the nature of a genomic library. The genomic library is necessary for the identification of newly discovered proteins.

The use of molecular analysis current technology allowed beginning the investigation of the expression of separate genes controlling the production of a definite protein. The analysis of gene structure helped understand their transcription mechanisms and identify many factors regulating it. In some cases these factors appeared to be hormones, in others – nucleoproteins responding extracellular cues.

The opportunity to investigate separate genes' functions appeared after the introduction into practice the method of obtaining transgenic animals and models with a definite gene knockout. Into the egg cell of animals (mice) separate genes responsible for the synthesis of a definite factor are introduced, and, as a result, animals with hyperexpression of this focalized tissue-specifically factor are obtained. The gene knockout technique is particularly widespread nowadays as it allows studying the role of separate factors in various diseases' pathogenesis.

The gene expression leads to the intensification of protein synthesis. The proteins can be detected and identified both by immunochemical method – with the help of gel electrophoresis, and by immunohistochemical methods – using high-specific antibodies.

The polymerase chain reaction (PCR) discovery in 1986 became a revolution in practical molecular biology due to the possibility of quick amplification of DNA specific fragments. For this method use it is enough to have one molecule or a DNA or RNA fragment to produce a necessary for the identification amount of DNA copies with the help of gel electrophoresis and Southern-blot- hybridization. This method is widely used for gene structure and expression investigation. For nucleic acids isolation and their conversion into the liquid phase cellular and tissual breakdown is necessary, and it complicates the comparison of amplification results and histopathological picture and also cell counting.

The in situ hybridization method provides an accurate focalization of specific nucleotide sequence in cells. Unfortunately, it possesses a low-grade (compared to PCR) sensitivity, and, to carry out the reaction it is needed not less than 10-20 m-RNA copies per a cell.

The use of molecular technology has allowed combining the high PCR sensibility and cellular focalization of in situ hybridization. This method got the name of in situ PCR.

All the three methods are widely used in pathology. The greatest number of the in situ PCR investigations is focused on the definition of viral or foreign sequence of nucleic acids. The possibility to detect latent viruses in single copies is an important measure on the way to viral disease pathogenesis comprehension.

The in situ PCR method is also used to study endogenic DNA sequences inclusive of single human gene copies, chromosomal translocations and mapping of numerically insignificant copies of genomic sequences in metaphase chromosomes. The possibility of carcinogenesis genetic determinants studying in-

cluding DNA mutations and chromosomal translocations is extremely important for the comprehension of latent period between DNA damage and the appearance of morphological signs of atypia or malignization.

The use of the complex of molecular-biological, immunological and morphological methods in pathoanatomy has lead to a more thorough understanding of the interconnection between the structure and the function, and to the formation of a new line in the development of pathology – functional morphology, which in XXI century is becoming a guiding approach in studying the human body and various diseases morphogenesis.

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IMMUNOLOGY BARRIER IN EPITHELIAL LAYER WITH MICROBIAL CONTAMINATION

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Mechanisms of the immune response in epithelial barriers of the body in response to microbial contamination, and also owing to the effect of other disturbing factors, are the subject of fierce disputes. Singular woks on the influence of regulator factors, in particular, cytokines, on the barrier properties of epithelial plates do not solve the problem of cell-to-cell cooperation between lymphocytes and epithelial colony-forming cells at alteration and microbial contamination (Yarilin A.A., 1999).

The biological sense of inflammation as an evolutionally formed process lies in delimitation and elimination of the lesion and causing it pathogenic factors. In the infant state of the infectious agent damage of the epithelial barrier a local inflammatory response progression occurs, redistribution of cells from the blood bed to the inflammatory tissue and intensification of proinflammatory cytokines output (Tsuboushi S., 1981). In the initiation and regulation of cellular and antibody responsiveness macrophages take part by antigen presentation to lymphoid cells and because of their possessing a powerful phagocytic and lytic potential, the presence phagocytotic vesicles in their cytoplasm, the ability to release compliment components and also various cytokines output. A macrophage is an elementary cell regulating regenerative processes by cytokines output, the transition from the inflammatory response and alteration of the epithelial barrier to its neogenesis (Yarilin A.A., 1996, 1997, 1999). At the same time the enzymes released by macrophages, proteolytic enzymes in particular, can damage surrounding tissues and give ride to secondary inflammatory alterations, thus promoting the process's chronization in the epithelial plates (Roncucci L., 1988). Macrophages influence cytodifferentiation, migration, poliferation and functions of monocytes, neutrophils and lymphocytes. In the focus of primary acute inflammation macrophages make less than 5% of infiltrative cells, yielding in number to granulocytes. On the second-third day from the beginning of alteration macrophages become a predominant cellular pool of the infiltrate, succeeding quickly tumbling granulocytes. The migration of monocytes from the blood flow into tissues is mediated by the expression of integrin adhesion molecules CD18+ , IL-6, INF- , TNF-a (Ohtsuka Y.,2001) on monocytes and endotheliocytes. After the adhesion to endothelial cells and successful cooping of the endothelial barrier by diapedesis and transepithelial migration, the monocyte makes land downstream the affected epithelium region or pocket of infection influenced by the corresponding chemoattractants. The chemoattractant function is performed by the components and decay products of microbes, the bacterial LPS in particular, and also the tissues' breakdown products (Paltsev M.A., 1996). The cells' movement with no such a gradient bears an irregular character and is called "random migration". When binding the LPS/LPB and the cellular form of myelocytes the cell eating of gram-negative bacteria is intensified, the cell-mediated response to low concentrations of LPS. When binding the LPS/LPB and the soluble form of CD14 a triple complex, which is identified by the receptors of endothelial, epithelial and dendritic cells of Langerhans, is formed, and then the induction of the inflammatory response to LPS occurs. Such reactions bear local character and prevent the incidence (Roncucci L., 1988). The binding of the LPS/LPB complex and CD14 monocytes can be over with the LPS internalization without the induction of the inflammatory process.

In the early stage of inflammation the bacterial LPS or the agent of viral nature, affecting epithelial cells, induce the release by epithelial cells of proinflammatory cytokines, IL-1 and TNF-a in particular (Bacon K., 1998). Besides, when damaging the epithelial barrier, macrophages, being antigen-presenting cells and affecting through the receptor apparatus of immunocompetent cells, induce them to release proinflammatory cytokines mediating the activation of specific and nonspecific immune responses, as well.

The number reduction of cells examined in populations' peripheral blood in the acute period of sickness at various virulent diseases attended by the damage and partial damage of mucous coats' and epidermis's epithelial plates cannot be interpreted as a being formed immunodeficiency disease, but should be considered as variable immunodeficiency, due to the fact that the number of immunocytes increases

within the local inflammatory nidus. The given phenomenon is considered as redistribution and activation of immunocytes with local inflammatory nidus in the body. In the opinion of Steinman R. (1999), at tissues' damage and local action of pathogens the regenerative processes are attended by a frank infiltration by lymphocytes, plasma cells, polinuclears, and singular eosinophiles. The author showed that with a pathological focus available, in case of need to release the regeneration process, the activation of lymphopoiesis and migration of lymphocytes from the immunopoesis central organs, which passed the antigen independent differentiation, into the regenerating epithelial plate. The immune cells' migration into the epithelial barrier and through it onto its surface plays an important role in immune and inflammatory processes.

The epithelial barrier's protective function in many ways is defined by the local immunity state, the interaction of the cells of the immune system of the epithelial plates' adjacent collagen structures, and also the number, spectrotype, potency of immunocytes, level of released by them cytokines and other cellular modulators.

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UPPER RIDGE DEFECT AUTOOSTEOPLASTY IN CHILDREN WITH CONGENITAL CLEFT LIP AND PALATE

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It is acknowledged that in treatment of this pathology a complex approach is necessary: stage repair, orthodontia, logopedia and a complex of rehabilitation actions aimed at the child's adaptation in the society [1].

In the nosogenesis of facial middle zone deflections in patients with congenital cleft lip and palate (CCLP) an important place is taken by: the congenital deflection of upper jaw bone, alveolar bone region upper jaw bone segment and bulb-shaped nasal opening diastasis conditioned in the ontogenesis and progressing in the postnatal period, lip-buccal and guttural ring myodinamic balance failure, disproportion of facial bone in bone sutures [2, 3].

Osteoplasty of the alveolar bone allows repairing these defects partially.

In the question of choice of time of carrying out osteoplastic operations surgeons have no agreement of opinion [4, 7]. We consider incontestable that for full dentition of canine teeth and their introduction to occlusion osteoplasty should be carried out in the period of transitional dentition. But practice testifies that after palatoplasty the upper jaw bone arctation influenced by the draft of cicatrized palatal flaps redoubles and the orthodontic care becomes more complicated. For bimaxillary protrusion autoosteoplasty in is advisable to be carried out in the closing stages of orthodontic care in the period of permanent dentition, and in the period of transitional dentition – to provide so-called promoting "swaying" of the upper jaw fragments in the transversal plane.

It is in our belief that the stability of well-timed orthodontic care results depends on the surgical interference algorithm, autoosteoplasty among them.

The purpose: of the present research is a comparative study of remote results of CCLP children alveolar bone autoosteoplasty carried out in the period of transitional and permanent dentition.

Methods: In the period from 2003 to 2006 surgical interferences on upper ridge bridgework in 29 children with congenital cleft lip and palate had been carried out. There were 12 patients of them in the period of transitional dentition, 17 – in the period of permanent one. All the patients were under orthodontic care. The problems of orthodontic preparation to autoosteoplasty – regular size and shape repair of dentoalveolar arch for the purpose of the upper ridge de-

fect real size determination and optimal occlusion contacts achievement.

Autoosteoplasty problems:

1 – to remove the alveolar bone imperfection and by this to stabilize the maxillary bone fragments alignment reached by the pre-surgical orthodontical preparation;

2 – to provide osteal support of the teeth located on the edge of the defect, that is absolutely important for the oncoming bridgework;

3 – to provide conditions for the oncoming rhinocheiloplasty in the region of bulb-shaped nasal opening defect, to create osteal support of the nose wing base, to eliminate the depression of the upper lip [6];

4 – to enlarge the maxillary bone apical basis for the protraction of the frontal denture on indications.

We have tried to analyse the autoosteoplasty results in CCLP patients taking into account:

1 – the alveolar bone defect degree (on the classification of Davydov B.N.) before and after the pre-surgical orthodontic preparation;

2 – the reparative-regenerative process degree after the autoosteoplasty on the classification of Bergland O. and co-authors, 1986;

3 – the method of pre-surgical orthodontic preparation (using dismountable and fixed orthodontic constructions);

4 – the age of a patient (early or late autoosteoplasty);

5 – the stability of orthodontic care results.

The surgical interference was carried out in all patients on the same method. A transplant bed separating the nasal cavity from the oral one in the oral cavity in the defect region was formed, after which the defect was filled with atomized bone got from the frank bone ridge. A part of the transplant was disposed over the whole surface of the frontal alveolar bone part for the purpose of the apical basis restoration, and also in the region of the nose wing base. The wound was sewn on account of local tissues mobilization. At large defects for the transplant closure a trapezoidal flap from the upper lip was used. Since 2005 the method of osteoplasty using thrombocytes rich plasma (TRP) has been introduced.

Besides the clinical estimation in the pre-surgical period and in the dynamics there were carried out:

1) the computerized axial tomography (CAT);
2) the ortopantomography;
3) the dental roentgenography;
4) the ultrasound investigation (USI).

Results: In patients with the follow-up periods up to 18 months the substrate in the CAT represented an intersection up to 3 mm thick. The substrate tissue density, on the densitometry data, is close to the bone tissue density (form 280 to 450 EH). For the comparison, normally this characteristic makes 550-800 EH depending on the bone layer (cortical plate, fungoid part). In 2 years the substrate looked as bone tissue with distinctly defined cortex and marrow space with the density from 450 to 640 EH. In all the case the substrate was disposed in the bulb-shaped opening region at the level of the upper third and alveolar bone middle connecting its segments with each other.

In one patient the transplant represented bony prominences along the edges of the segments without bounds between them.

At the US-investigation in all the patients in the region of the maxillary bone segments' diastasis the cortical plate continuity was observed. The diastasis width according to the USI and CAT data in the pre-surgical period fitted together.

In all the patients the upper lip had regular contours without natural for this anomaly flattening on the non-union side and without the nose wing base depression. At the ambilateral non-unions the intermaxillary bone was motionless. At the reparative rhinoplasty carrying out in the region of bulb-shaped opening intraoperatively an osteal regenerate was defined in 14 patients.

The data got allow considering necessary the alveolar bone bridgework for its continuity restoration, creating conditions for homogeneous maxillary bone development and soft tissues support, that makes the correction surgeries carrying out easier. In the period of permanent and transitional dentition the regenerate formation has no differential peculiarities. That is why an early carrying out of the surgical interference creates favorable conditions for the maxillary bone development and correct dentition and the introduction of permanent teeth, canines first of all, to occlusion. The main criterion for the interference carrying out is the orthodontic readiness of the patient. The full height alveolar bone bridgework problem remains open.

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Shot reports

SMOOTH MYOCYTES IN THE THORACIC DUCT VALVES

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Condition of the problem**.** The opinion, that valves are not contain the myocytes in their cusps and are moving passively by the gradient of vacillating lymph flow is prevail in the literature [2]. Isolated messages testify to inverse. Y. Kajawa [1] have found that longotudinal muscular bundles jut out deep to the central plate of the thoracic duct valves. Used the histological and electron microscopic method of unvestigation, H. Ohemke [3] have described the smooth myocytes in the valvar cusps of human foot lymphatic vessels. Smooth myocytes form accumulations in the base of a lymphatic valve – its muscle which become thin in the cusp [4].

Take into consideration a key role of valves in the organization of lymph outflow from organs, it was decided to fulfil the investigation with the aim to identify the smooth myocytes in cuspes of the thoracic duct valves.

Material and methods. The work was carried out on both sexes human cadavers of 17-40 years old, who have died from casual reasons without pathology of cardiovascular system (30) and bothe sexes white rats of 5-12 months old (30). Thoracic duct was allocated without a preliminary injection, it is longitudinal dissected and choosed cusps of its valves. Material was fixed in 10% solution of neutral formalin, stained in paraffin with following production of serial longitudinal and transverse sections of 5-10 mkm in thickness. Sections were stained by picrofuxine, azane, orseinum. For specific identification of smooth myocytes in human thoracic duct the material was processed by Human Alpha Muscle Actin (monoclonal antibodies RTU-SMA, Novocastra Laboratories), contained the antibodies to α-actine of vascular smooth myocytes, and diaminobenzydinum, then poststained by hematoxilin. Smooth myocytes in thoracic duct valves were discovered by histochemical method (staining by benzydinum on myoglobinperoxidase witn poststaining by hematoxilin-Fe and without it) and with electron microscope.

Figure 1. Thoracic duct of a man, longitudinal section: 1 – longitudinal muscular bundle in intima; 2 – radial muscular bundle enters into cusp of a valve. Picrofuxine. x 400.

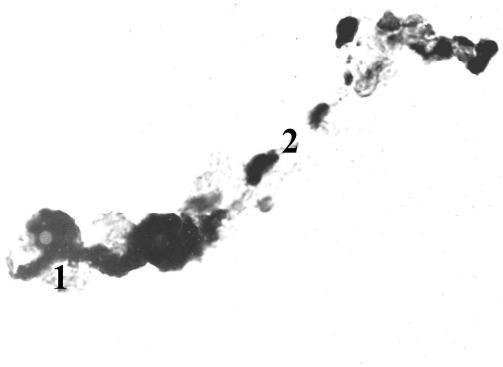

Figure 2. Cusp of a human thoracic duct valve, longitudinal section: 1, 2 – longitudinal & transverse orientated smooth myocytes. Immunohistochemical method. x 600.

Results. The heterogenous construction of valves is discovered on the histological sections. Their parietal surface is covered by thickened endothelium, nuclei of its cells are orientated oblique-transverse, situated frequently; on the axial surface – infrequently, longitudinal, by the direction of lymph flow. The plate of loose connective tissue of different thickness is situated between two thin layers of endothelium. Fold-

ing bundles of the collagen fibers locate in its more wide parietal part. They are straightening during widening of the valvar sinus under the indirect lymph flow pressure. The connective tissue fibers are more thin in an axial part of the cusp, here there are more elastic fibres. Myocytes of the vale have, more often, transverse and oblique-transverse orientation. Longotudinal and oblique-longitudinal myocytes are determined mostly in the axial parts of valves. Middle (muscular) coat become more thick and forms a protuberance in the base of valve towards its cusp. Longitudinal muscular bundles from intima of usually distal, prevalvar segment of the thoracic duct turn and enter the axial sector of cusp (Figures 1, 3), where internal elastic membrane is saved. It is loosend and disappears in the parietal sector of cusp.

The compactness of myocytes allocation in the valvar cusp 3-4 times less than in valvar roller (parietal bulge), where more large myocytes and their bundles form the muscular sheet in 2-4 layers. In cusp the myocytes are more or less dispersed and form the network of different density. It is nice shown after staining on myoglobinperoxidase: grains of benzydinum are dissipated in the cusp and form compact accumulations in the base of valve. Myocytes are completely colored in brown after immunohictocemical processing, in other cells – only nuclei in pale blue by hematoxilin (Figure 2).

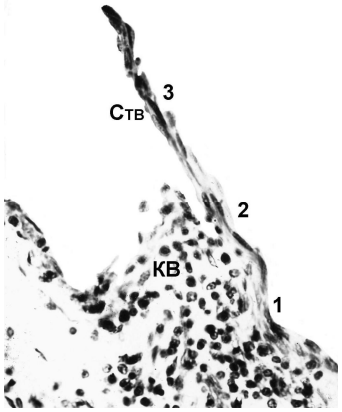

Figure 3. Thoracic duct of a rat, longitudinal section: КВ – valvar roller; Ств – cusp; smooth muscular bundle from intima (1) enters into a valvar roller (2) and a cusp (3). Picrofuxine. X 600.

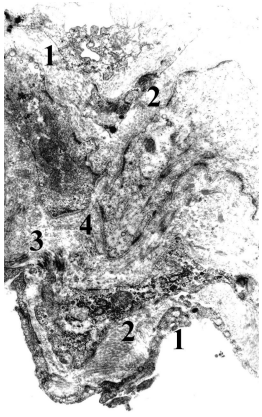

Figure 4. Cusp of valve of a rat thoracic duct, electron microscopic picture: 1 – endothelium; 2– connective tissue cells; 3 – collagen fibers; 4 – smooth myocytes. x 7500.

On electron microscopic figures the connective tissue cells and fibers are revealed under two layers of endothelium of the rat thoracic duct valvar cusps and deeper – myocytes (Figure 4). They have a basal membrane, their cytolemmas are hardly deformated by caveolas.

Conclusion. Thus, muscular bundles are discovered in the human and white rat thoracic duct valves. Proper smooth myocytes of valvar cuspes increase their viscoelastic properties, stability to alternating pressure of lymph flow, determine the capacity to the shape and location autoregulation. Myocytes are heterogenous distributed in valves. Their lesser numbers and sizes in cusp correspond to its more high mobility; increasing of longitudinal myocytes and elastic fibers content in axial sector – to shocks of direct lymph flow. Muscular bundles from valves continue into adjacent parts of the thoracic duct walls. It is possible to assume the active, coordinating movements of the valves and muscular cuffs of lymphangions, including the procesees of openung an closing of valves.

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THE PRESENT CONDITION AND PROSPECTS OF COAL SECTOR IN THE WORLD FUEL AND ENERGY COMPLEX

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The article gives the statistics of coal as one of the basic natural mineral resources. It is considered the situation with stocks of oil in regions and countries, the dynamics of its extraction, consumption, export, import, average year prices and the present state of the coal-mining branch. It is also analyzed the prospects of world coal sector in the near future years.

Coal has been a basis of the world fuel-energy balance for a long time. It surpasses in a total energy, it comprises, all the rest of fuel-energy resources taken together.

The world confirmed mineable reserves of this kind of raw materials make up 982,7 milliards of tons, including black coal – 518.2 milliard of tons and brown coal – 464,5 milliard of tons [1].

The world provision with coal explored reserves is as a whole high– 200 years [2].

The biggest total coal reserves are in the USA (246643 mln.t.), Russia (193771 mln.t.), China (114500 mln.t.), India (94620 mln.t.), Australia (97300 mln.t.).

The data on coal mining capacity in the world are represented in Table 2.

Table 1. Reserves of all kinds of the confirmed mineable coals on 01.01.2004 (mln.t.) [3,4]

	Total	Brown coals	Black coals
Europe (with Russia)	285596	159304	126292
Asia	266887	76278	190609
Africa	55093	347	54746
America	317347	151095	166252
Oceania and Australia	97873	42038	55835
Total	1022795	429061	593734

Table 2. Dynamic of the all-type coal mining (mln.t.) [3,4]

	1995	1997	1998	1999	2000	2001	2002	2003	2004
Europe (with Russia)	1177,1	1113,5	1052,4	1017,6	1024,8	1045,2	1012,2	998,5	977,2
Asia	1950,3	2036,5	1885,6	1632,2	1626,9	1803,4	2069,4	2326,0	2699,4
Africa	214,6	227,7	231,4	231,1	231,5	229,9	227,4	242,6	242,0
America	1061,4	1121,5	1145,4	1126,6	1106,9	1157,3	1134,6	1106,1	1158,2
Oceania and Australia	248,0	278,5	291,3	297,1	314,2	335,4	344,2	354,7	359, 8
Total	4651,4	4777,7	4606,1	4304,6	4304,3	4571,2	4787,8	5027,9	5436,6

Leading countries in miming all-type coals are (according to 2004 survey, mln.t.): Germany (211,05), Poland (161,21), India (402,5), China (999,17), the Republic of South Africa (225,3), the USA (976,72) and Australia (310,62).

The above mentioned countries are very likely to remain the main coal producers. More over, China is planning to increase annual mining capacity up to 2.0 milliards of tons by 2010, and the USA – up to 1,4 milliards of tons. There is also a growth trend of the coal mining in Columbia, Venezuela, Indonesia, Vietnam.

At the same time (during the same period) coal mining capacity in Europe is re-

ducing. The biggest decrease in production is in Great Britain (by 22%) and Ukraine (by 21,7 %).

While coal consumption in Europe, America and Oceania with Australia is practically stabilized both in the region as a whole and in each country, there is a growth trend in its consumption in Asia and Africa. The largest coal consumption was in China during 2000 - 2005 (increase by 108 %), Indonesia (by 103 %), South Korea (by 27,7 %), Japan (by 27,7 %), India (by 22,6 %), Kazakhstan (by 17,2 %).

Table 3. Dynamic of all-type coal consumption (mln.t of standard fuel) [3,4]

	1995	1997	1999	2000	2001	2002	2003	2004	2005
Europe (with Russia)	781,5	736,4	688,7	662,6	669,7	657,5	695,2	678,1	673,6
Asia	1498,6	1599,4	1380,7	1395,6	1411,4	1637,3	1873,5	2202,5	2387,0
Africa	122,5	130,8	128,0	118,9	120,1	121,6	131,9	139,8	136,0
America	797,4	850,3	939,5	909,9	901,2	894,6	872,9	915,7	231,5
Oceania and Australia	62,4	70,4	68,5	71,7	71,9	74,7	76,4	80,0	79,8
Total	3262,4	3387,3	3205,4	3158,7	3174,3	3385,7	3649,9	4016,1	4207,9

According to the forecast of the international energy agency (MEA) coal consumption will stably grow up to 2030. On average, demand for coal during 2000-2020 is going to increase by 1,4 % annually. By 2030 the world needs of coal will have made up 7,3 milliards of tons and will provide 22 % of the demand for energy resources [5]. This is explained by expected increasing needs of power industry. One more important conclusion: India and China will have 80% of the increased demand for coal to provide the energy balance [6].

A geographical structure of the coal consumption is also going to change in the nearest decade. Demand for coal will rapidly increase during 2000-2020 in developing countries, as well as in countries with transition economy in Asia, the Near East, the Middle East, Latin America (by 2,8 % annually). As a result by 2020 a unit weight of Asian countries in the world consumption will have made up 49 %, in 2030 – up to 54 % (in comparison with 40 % in 2000). By 2020 the share of OECD countries in the total coal consumption will have reduced by 37 %, by 2030– by 32 % (2000 – 46 %).

Table 4. Dynamic of export and import of black coal (mln.t.) [3,4]

		1995	1997	1998	1999	2000	2001	2002	2003	2004
Europe (with Russia)	Exp.	78,2	66,1	67,9	67,3	82,2	86,6	82,1	94,9	98,8
	Imp.	193,0	197,0	192,3	167,5	209,1	230,0	212,8	233,0	236,6
Asia	Exp.	84,9	102,3	108,3	112,7	142,7	189,1	186,7	208,4	229,0
	Imp.	244,5	275,1	268,6	273,0	320,7	332,6	368,5	382,9	249,6
Africa	Exp.	59,7	59,0	62,2	66,6	69,9	66,7	61,7	71,5	67,8
	Imp.	5,4	5,5	5,4	5,0	6,2	8,2	6,9	5,2	20,8
America	Exp.	136,6	144,1	139,3	122,2	128,9	120,0	101,5	110,6	119,6
	Imp.	34,7	42,4	46,8	45,1	54,1	63,3	61,2	67	64,4
Oceania and Australia	Exp.	137,5	159,0	168,2	172,8	186,8	194,0	203,9	207,7	223,7
	Imp.	0,2	0,4	0,5	0,4	0,3	0,3	0,3		
Total	Exp.	496,9	531,5	545,9	541,6	610,5	656,4	635,9	639,1	738,9
	Imp.	477,8	520,4	513,6	491,0	590,4	634,4	649,7	688,1	571,4

The dynamic of the world import and export of coal is illustrated in Table 4.

The biggest part of coal is used in countries-producers, nevertheless, the world commerce capacity of coal continues to grow.

Principal coal importers are Japan (179,8 mln.t. in 2004), Germany (41,6 mln.t.

in 2004), Great Britain (36,1 mln.t. in 2004) and the USA (24,7 млн.т. в 2004 г.).

Leading exporters are Australia (223,7 mln.t. in 2004), Indonesia (105 mln.t. in 2004), China (102 mln.t. in 2004), Russia (72 mln.t. in 2004).

Significant changes in a branch structure of coal consumption are also expected. The demand for coal from power industry sector is going to increase the most rapidly. This branch share in a total consumption of black coal will increase up to 79 % in 2030 (in comparison with 69 % in 2002). This will in long-term outlook be caused by an expected rise of coal competitiveness in comparison with other types of fuel, taking into account a forecasted more slow price growth.

Table 5. Branch forecast for coal consumption [7]

	2002	2030
Total	100	100
Power industry	69	79
Industry	16	12
Housing complex	3	1
Прочее	12	8

From the table we can see that coal consumption in industries will decrease and its unit weight in the total coal consumption will have reduced by 2030 by 12% (in comparison with 16% in 2002). Demand growth for industrial coal (coking coal, first of all) will make 0,5 % annually. At the same time, a trend of coal consumption reduction and its replacement by gas application in industries of OECD countries will take place. While the demand for coal in developing countries will be increasing as a result of demand growth from the heavy industry, first of all, from a ferrous metallurgy sector. Use of coal in domestic and commercial sectors will also decrease, most rapidly in OECD countries.

A keen change in the structure of orders made on turbines for electric power stations testifies preference towards coal used as a fuel. Whereas in 1997-2001 about 60% of orders for equipment were the orders for gas stations and 25% - for coal stations, 40% are orders for turbines for coal electric power stations, and a share of orders for gas stations will reduce up to 25% within the next decade [8].

Coal consumption by electric power stations started to grow a few years ago, which was caused by economical reasons, - an average price for gas per standard fuel unit is twice as much as for coal.

The majority of countries with a stable economy, prices for coal (in an equivalent ratio) are essentially lower than prices for gas and oil products. That is why in the world economy coal is more preferable rather than any other types of fuel. Thus, the share in generation of electrical energy from coal in the USA, the country with the most strict market economy, is 52%, in Germany, the country with a socially-oriented economy, – 54%, in Russia – 26%, in China, the country with a transition economy – 7% [9].

Nevertheless, according to analyst opinion, it is quite difficult to switch from gas to coal. And this switch will not be large-scale. First of all, transition of electric power stations from gas fuel to coal fuel is not cheap. Secondly, public opinion will always be against it because of ecological reasons.

Anyway, transition of electric power stations from gas to coal may last 10-20 years and shall be considered as a problem of future.

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SYSTEM DATA PROCESSING RELIABILITY ANALYSIS OF ROUTINE PROBLEMS IN THE APM WIN MACHINE SYSTEM IN WINDOWS VISTA

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The computer aids data processing reliability should be considered as a quality spread out in the course of time. With the new Windows Vista operating system début on the 30th of January, 2007, there appeared an opportunity to use all the might of modern hardware electronic equipment (quad-core processors, powerful high-speed on-board buses, display cards with four-way subsystems, 1 T-byte Winchester disk). The new Vista technologies enable to level up the output and reliability of the system radically. The SuperFetch technology accelerates the computer work by means of data preload. The SuperFetch service is constantly working in the background, analyses programs' work objective laws and fulfils the data preload which can be needed in the earliest possible timeframe. With the help of the ReadyBoot technology the system work is accelerated on account of USB flash-drive mapping and using it for temporary files storage. The Windows Ready Drive reduces the energy consumption and speeds up the notebook computers' work hybrid hard disks. These Winchester disks have additional flash-memory modules which are used by the system for temporary file storage and sleep schedule work. In the event of a refusal the stuffing and renewal center reliably customizes automatic file stuffing and creates the archived image of all the hard disk, and the shadow copying technology effectively restores documents' previous versions and the data within the APM Windows WinMachine system. The new technology of Windows Vista installation is performed of prearranged images accelerating by this the installation process itself and reduces errors occurrence probability, and all the recovery facilities can be activated from the setup DVD.

The Windows Vista operating system is more secure than the Windows XP SP2 one regarding safe problems as it contains a range of new security facilities. The UAC (User Account Control) facility prevents illegal application preferences, system variables changes and other interferences into the system work. The security service center controls all the computer security main variables: auto update, fire wall, antivirus and antispy programs, user account and Internet Explorer 7 monitoring service. The Windows protector utility grants the protection from various hostile programs. There is a facility to restrict the access of naïve users to the computer. A built-in fire wall Windows Vista guarantees an efficient protection of the computer from an unauthorized entry through the local network or Internet. The bidirectionality of the fire wall protects from an outside intrusion and allows prohibiting unauthorized data transmission from the computer to the Internet. A new system work watch facility is the reliability and productivity monitor consisting of three components: assets monitor, system monitor and system stability monitor, provides the system reliability monitoring at data processing by WinMachine. The assets monitor controls the four subsystems reliability: the CP (central processor), disk, net and memory. In the CP line chart one can watch the processor loading and clock speed change. At little loading the monitor automatically reduces the clock speed, that can be visually estimated as the reliability of this technology. The disk status line chart demonstrates the acting speed of the data interchange with the hard disk. In the net chart the data interchange speed in the net and every command characteristics are reflected. In the memory chart the process of the RW memory using and the amount of errors when addressing to page frames. A great amount of errors testifies to an insufficient RW memory capacity to perform complex computations (for example, the computation of a camshaft mechanism with translation roller lifter in the APM Cam assembly unit) and that the necessary information has been read from the swap files. The system monitor watches the computer's fail-safe operation displaying its numerical values, various charts and diagrams. The system stability monitor controls the system stability options and records various events influencing the stability. On the ground of this data the system stability index, which is displayed in the chart in the form of common errors, load errors, hard disk and RQW memory failure, failures, starvations and forced close-downs of APM WinMachine, is calculated. The Windows Vista operating system for the first time has got an opportunity to encrypt files and folders in the level of file manager. For the encryption provision the file manager EFS is used. At that the best way of encryption is the folder encryption. With the help of the new technology BitLocker one can encrypt a whole disk partition. This guarantees a higher security and reliability level.

Thus, the computer high information processing reliability is provided by the new technologies Vista for the system survival, automatic repair after various failure kinds in PC devices, reliable security from hostile programs' effect and desired protection from unauthorized intrusions with getting high performance of computations when solving different problems.

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Shot report

FRACTAL MODEL OF MICROACCELERATIONS: RESEARCH OF QUALITATIVE COMMUNICATION{CONNECTION}

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In work qualitative connection between fractal dimension of Weierschtrass-Mandelbrot function and the moment of operating rocket engines spacecraft is researched.

The problem of microaccelerations during more than thirty years is deep a barrier on a way of development revolutionary new technologies [1]. First were confronted by it the American researchers in 1973, 300 various series which have developed and realized more experiments at space station " Skylab " from which not all have come to the end successfully. Later it has been found out that the reason of some unsuccessful experiments became excessively high level quasi-static components of microaccelerations.

The analysis of conditions of flight has shown that the condition of weightlessness inside of a spacecraft in space is not absolute because on it not compensated system of forces and the moments works. Therefore in all internal space spacecraft there is a field of residual small accelerations which can be named microaccelerations. Studying, forecasting and maintenance of a level of microaccelerations necessary for technological processes became one of the major problems of space materiology.

Technologists have started to struggle with quasi-static components microaccelerations trying to improve the design-layout circuit (DLC) of spacecraft. For this purpose tests for orbital complexes «Salut-6,7» and also a number of experiments on an artificial satellite of type the PHOTON were spent. The researches connected with microaccelerations were spent and abroad: the program onboard orbital space stations (OSS) «Freedom». The striking example of successful struggle with quasi-static components became spacecraft «Spot-4»: it included one panel of the solar battery (PSB) which fastened to case spacecraft by means of an elastic bar. «Spot-4» has not been intended for power-intensive processes.

The idea maintenance of the necessary level microaccelerations not in all internal space spacecraft and in a working zone of the process equipment now is considered one of the most perspective. The topical of the this idea increases in connection with planning in RCC "Energy" of the technological project "OKA-T" the level of microaccelerations on which should not exceed 10^{-7} g.

Not less important than experiments the role at the present stage of development of a problem microaccelerations plays mathematical modelling. For achievement of more effective results is reasonable to spend natural tests in a complex with mathematical modelling.

There are great number of the mathematical models estimating a level of microaccelerations onboard spacecraft after its flight, however until flight estimations are far from perfect.

Developed by authors the fractal model of microaccelerations with use of the valid part of Weierschtrass-Mandelbrot function (WMF) [2] allows to estimate a level quasi-static components of microaccelerations onboard spacecraft without obvious modelling its movement. Following statement of a task is used: rotary movement spacecraft around of the center of weights is considered, the level of the microaccelerations arising from fluctuations of elastic elements after individual abrasion of operating rocket engines of system of orientation spacecraft (ORE) is estimated.

During modelling an identification of parameters WMF and characteristics of physical conditions at which the field of microaccelerations inside of a working zone of the process equipment is created at carrying out on spacecraft various experiments is one of the key question.

In the given work the question of an opportunity of an estimation of average value WMF at a qualitative level is considered. For reception of average value of microaccelerations spatial rotation spacecraft of type «NIKA-T» having three elastic elements (model [3]) was considered.

The estimation of correlation was spent by classical factor of correlation [4].

Dependences of average value of microaccelerations on ORE moment for various values of the accelerative-mass characteristics spacecraft received on model [3], are resulted on fig. 1.

It allows to accept confidently a hypothesis about linear correlation between average value of microaccelerations and average value of WMF on 5 %-s' significance value (critical statistics 0,537). However the classical criterion is unstable to displacement from the normal law of distribution therefore to a final conclusion about applicability WMF for an estimation of average value of microaccelerations we shall apply nonparametric rank criterion Cox-Stuart′s [4].

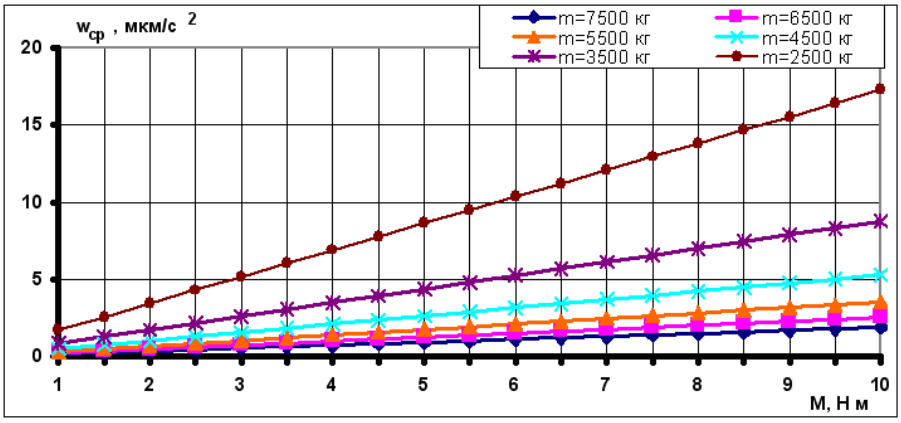

Figure 1. Dependence of average value quasi-static components of microaccelerations from moment ORE for various lump spacecraft

Dependence of average value WMF on its parameters is presented on fig. 2.

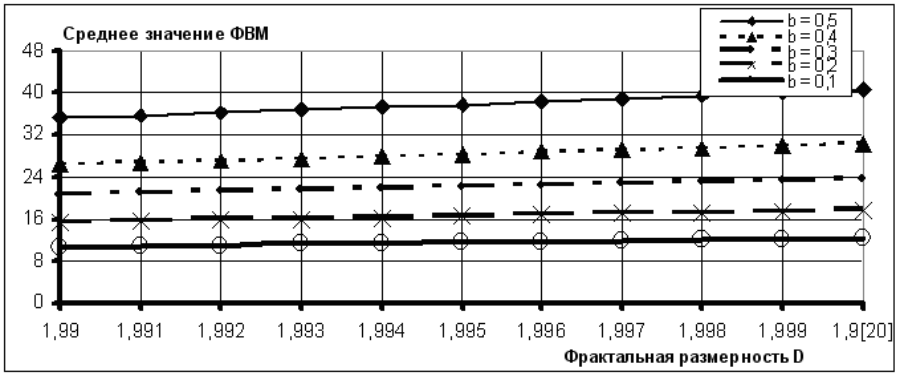

Figure 2. Dependence of average value WMF on it fractal dimensions at various values of scale parameter

The analysis shows that values of correlation coefficient is within the limits of from 0,80 up to 0,90 for various samples (fig. 3).

Figure 3. Values of correlation coefficient for various

For sample in 17 points it has the maximal value +17 at critical statistics for 5 %-s' significance values +9 [4] therefore the hypothesis about linear correlation is accepted. Similar results can be received considering other samples and researching correlation between dependences fig.1 and fig.2.

Thus by correlation coefficient and criterion Cox-Stuart's the opportunity of modelling average value

quasi-static components of microaccelerations by WMF in the statement designated above is proved.

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A NEW ELEMENTS OF EDUCATION PROGRAM AT THE PERM STATE UNIVERSITY FOR CREATIVE PALEOTECTONIC ANALIS FOR GAS AND OIL GEOLOGY

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Quality of education and preparing the specialists in the university is a subject of interests of not only high school representatives, but also that geological organizations, in which they work after getting the diplomas. So in the Perm State University are led work, which summery several directions: 1) improvement of methods fundamental geology and stratigraphy studies; 2) using the leading scientific technologies adjacent for the geology; 3) using three-dimensional computer modeling; 4) account of regional forecasts of oil and gas; 5) account of requirements of geological production on studying history geotectonic and oil content at local structures.

Study of influence reef-building Bryozoa and algae of artinskian stage of the Permian System on regularities of lateral changing for thickness of stratas was used as a model for the development of creative paleotectonic analysis of stratas with reefs at the PreUrals. Essence of method: 1) map-development of series of paleostructures maps (or maps for thickness of stratas) for one territory, but for several adjacent stratigraphic subdivisions *first* on stratigraphic refeathers all *without excluding* the bore holes; 2) map development of paleostructures maps *for same territory* and for *same stratas*, **but** without bore holes with reefs; 3) investigate for reef facies; 4) full paleotectonic analysis for all stratigraphic intervals of investigations.

This strategy allows reveal "reefs" on anomalies of thickness some stratas, even though it was not recognized on the traditional maps of stratas thickness, in that events particularly, when "reefs" was not recognized or is not identify on core-samples from boreholes bore holes. Elaborate regional tectonic and paleotectonic maps of the territory. This method can recognizes single-line structures, which are the most perspective for the searching for local oil and gas traps in reef-rocks of Devonian and Carboniferous stratas.

These creative exercises are updated by part of the classical course analysis for students, possibility, which greatly increase with using the computer technologies. These methods are use on the geological production.

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CRIME AS A TYPE OF ANTISOCIAL BEHAVIOR OF WOMEN IN RUSSIA

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It is evidently that one of the most dangerous types of deviance is crime. Scientific investigation of this problem found itself at the close of the XIX-th century. In early 70-th the problem was in hand of M.V. Duhovski, I.Y. Phoinizhki, K. German, M.N. Gernet, S.V. Poznyshev, P. Sorokin and others. But at the beginning of XX-th century all sociological studies were outlawed. As the result of this, problems concerning crimes were handled mainly in field of criminal law. The rise of sociology in Soviet Union, that took place in 60-th years of XX-th century, promoted the renewal of sociological studies of deviance. There are different sides of crime were widely investigated: minor crimes, rape crimes, victimology, ecological crimes and others. The most important in this sphere was contribution of S.S Alekseev, U.M. Antonyan, M.M. Babaeva, S.V. Borodina, S.G. Gerasimov, Y.I. Gilinski, K.K. Goryaninov, S.V. Diakov, A.G. Zdravomyslov, V.N. Kudryavzhev, V.V. Lunev, A.A. Gabiani and others.

Explaining crime many specialists repeatedly paid their attention to the large complex of outdoor factors (for instance biological, sociological, economical and so on). That is why the challenge of crime is an actual point not only among sociologists, but also among representatives of other scientific disciplines. Thus, for example, Italian criminalist Ch.Lombraso was one of those who examined entire system of factors, determining crime. Besides, he was the first one who tried to find out the reason of women's crime that was repeatedly investigated in other countries.

The problem of female crime wasn't the point of studying in Russia, inasmuch as it appeared that less crimes in Russia committed by women then those committed by men. Thus, for example, in 1897 only 15% of convicted were women, though the main plenty was 106387 people[1]. It is also known that women may drift into crime, but they only rarely pursue criminal careers. Many scientists considered such position to be bounded up with weak social activity of women in pre-revolutionary Russia.

But if to judge about the female crime in common, the rise of crimes among women is evident, despite the fact that the weight of it continues being stable and keeps 10 – 18% level. Though, for example, 178 crimes in 2005 were committed by women (it comes 13,7% to total amount of people committed crimes)[2]. At that, plenty of scientists consider felo-

[1] Source: D.A. Lee Crime as a social phenomenon. Moscow., 1997 p. 121 - 122
[2] www.mvdinform.ru

nious behavior of women to be caused by their emancipation. Though, it recently was accepted to think that the main reason of antisocial behavior of women was their wish to provide for their family.

Historically in all communities female labor has been resulted as hard and poorly-paid as compared with men. So evidently that such types of crimes as prostitution and theft are spread among young women. The fact is that low property level always made women cut many attractive values of modern youth down: fashionable clothes, clubs, parties and so on. Undoubtly, it causes feel of infringements and deeply jaundices women. This fact quite often makes them commit crimes concerning mercenariness or prostitution. Thus, for example, according to official statistics of MIA of late six months of this year there were committed 125591 crimes by women; 8548 of them are under age[3].

Secondary role among crimes in Russian Federation belongs to diffusion and using drugs and psychotropic agents, so as their analogs. It sharply concerns such boundary inhabited localities as Astrakhan region, because it stands as transit of narcotic drugs from Middle Asia to Europe. As a rule, drug transportation puts into practice with the help of autotransport, train and by ship through Caspian Sea (for example Turkmenbashi – Astrakhan)[4].

According to statistics, middle percentage of crimes, committed on the territory of Astrakhan region concerns 0,2%. Among them 6,9% Astrakhan women commit crimes. Almost all delinquents are women of 16 and more years old. According to the level of education, the largest part belongs to women with school (63%) and college education (21%), and then there are women with higher education (3,5%). As always, common mass of junkies belongs to women without confident source of profit, among them 1,3% of pupils and 1,6% of students.

Coming back to the problem of female crimes, it's necessary to notice, that its difficulty and incurability is stipulated by difficulties in process of resocialization that is much harder to overcome for women then those by men. Also a women committing crimes has the most dangerous influence on society. It causes invaluable development of family where the most important role in bringing up new generation belongs to a woman. That is why the problem of female crime is the most actual nowadays and demands especial attention of government and society in general.

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[3] www.mvdinform.ru
[4] http://atlas.socpol.ru

RHIZOCTONIA И GAEUMANNOMYCES SPECIES COMPOSITION UNDER THE CONDITIONS OF WESTERN SIS-CAUCASIA

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Western Sis-Caucasia root rot pathogen population has been studied at Krasnodar Lukyanenko Research Institute of Agriculture for three decades. It is presented by the following genera: *Alternaria, Pythium, Helminthosporium, Wojnowicia, Fusarium, Cercosporella, Gaeumannomyces, Rhizoctonia*, which have various occurrence frequencies on winter wheat. The share of *Rhizoctonia* fungi has been reported to exceed in frequency all other pathogens. The *Rhizoctonia* fungi, causing root rot on winter wheat, include several species: *Rhizoctonia solani* Kuhn. Teleomorph - *Thanatephorus cucumeris (A. B. Frank)* Donk, *Rhizoctonia cerealis* Van der Hoeven. Teleomorph - *Ceratobasidium cereale* D. Murray & L. L. Burpee *(*Anastomosis – *AG-D.) u Rhizoctonia oryzae* Teleomorph - *Waitea circinata* var *oryzae (*Anastomosis WAG-0*); Rhizoctonia zeae* Teleomorph - *Waitea circinata* var. *zeae (*Anastomosis WAG-Z*),* and *p. Gaeumannomyces - G. gramynis* var *tritici, G.graminis* var *avenae u G. gramynis* var *graminis.*

Rhizoctonia fungi have been widely studied on grasses, since they tend to cause serious damage to the plants covering golf-links. On grain crops these fungi have been observed in the USA by D.M. Weller et al. (2002), R.J. Cook (1981), R.W. Smiley and D.E. Wilkins (1992), A. Ogoshi (1987), in Australia by J.S. Gill, K. Sivasithaparam and K.R.J. Smet-Fem, in Germany (especially on malting barley), in Turkey by E. Demirci, C. Eken and H. Zengin (on sorghum), in Korea by Dong-mei Li, Ke-qiang Cao (2001), in Japan by T. Tsukiboshi and T. Kimigafukuro (1993). They have mostly identified *Rhizoctonia solani*, and less often *Rizoctonia cereals* or *Rhizoctonia oryzae*.

In the Ukraine in the 1970-s root rots on grain crops have been considered to be caused by *Rhizoctonia solani*, but more recently the pathogen have been proved to be *Rizoctonia cereals*. According to the Russian researchers Dolzhenko, Zdrazhevskaya, Burkova et al. (2003), in the Northern Caucasia root rots on grain crops are caused by *Gaeumannomyces, Fusarium* and *Pseudocercosporella* sp. Vlasova, Nikitina and Zhukova (All-Russian Plant Protection Institute) reported in 1995 that in Rostov region root rots on grain crops were caused by Fusarium-Pseudocercosporella fungi.

In recent years *Rizoctonia* sp. have been occurring on winter wheat more and more often, while in the 1970-s this pathogen did not even damage cereal crops. Z.A. Bochkareva and L.N. Tarasenko reported in 1974 that root rots were caused by fungi belonging to *Fusarium culmorum, F. sporotrichiella, Ophiobolus*

graminis, Wojnovicia graminis and *Helminthosporium sativum*.

Gaeumannomyces fungi have first been described in Australia in 1852 (154 years ago).

S.D. Garrett (1981), H.E. Nilsson and J.D. Smith (1981), D. Hornby (1998), R.J. Cook and D.M. Weller (1987) are among those numerous scientists who have been studying fungi belonging to this genus.

According to Garrett, grain crop diseases caused by these fungi are spread wherever these crops are grown in temperate and arid zones under irrigation. This disease has been admitted the most devastating disease damaging cereals.

The material has been collected during route inspections carried out jointly with regional and local plant protection stations. Pathogens were isolated in accordance with the conventional methods adopted in mycology using selective media.

Our studies carried out at KNIISH in the 1980-s revealed a small share of *Rhizoctonia* sp. (2-5%) in the complex of pathogens causing root rots. In 1990 their occurrence frequency in the northern part of the region (farm "Rossia" Pavlovskij area) averaged 3%; in the central part (farm "Rodina" Ust-Labinsk area) – 5.1-13.1%, in the southern sub-mount part (farm "Nasha Rodina" Gulkevichskij area) – 1%.

Our research has shown that the share of *Rhizoctonia* fungi in the Western Sis-Caucasia has been steadily growing compared to other pathogens. In Krasnodar region the share in 2000 accounted for 16%, in 2001 – 26.2%, in 2002 – 33%, in 2003 – 36.5% in 2004 – 38% and in 2005 – 40.5%. In the last years the rate of growth has slowed down from 10.2% in 1999-2000 to 2.4% in 2004-2005.

The visual symptoms of *Rhizoctonia* disease on cereal crops include thick brown coating of mycelium and sclerotium covering the root surface. The damaged tissue gets brown. This type of damage is also characterized by distinct eye spot. Ellipse-shaped light spots emerging at the base of leaf sheath and straw have distinct dark-brown edges, which help to distinguish them from *Cercosporella* spot disease. The spots which appear mainly on leaf sheaths may reach 15-25 mm in length. The major sources of primary infection are usually *Rh. solani* sclerotia accumulated in soil and mycelium contained on plant residues. The sclerotia maintain their viability in soil for two years. The major role in disease development belongs to the fungus mycelium, which is characterized by intensive growth. Under favorable climatic conditions (darkness, humidity up to 95% and air temperature 28-30^{o}C) the infection quickly spreads to the upper parts of plant, including leaf blades, and even to the neighboring plants. Mycelium fragments may be dispersed to long distances by wind and cause new infection.

According to the data of the International Rice Growing Institute, there exist no sources of immunity. Rice varieties, which are resistant to *Rhizoctonia* at the sprouting stage, may become susceptible at the stage of maturation and vice versa. In the Russian Federation the problem of winter wheat resistance to *Rhizoctonia* fungi has not been studied, neither were studied the strains of the fungus causing *Rhizoctonia* root rot on cereals.

In our studies *Rhizoctonia* fungi have been isolated on root rot damaged winter wheat plants grown after all studied previous crops but for fallow. In Rostov region the frequency of these fungi on plants grown after winter wheat varied between 1 and 19.5%, after peas – between 0.5 and 5.5% and after corn – between 3 and 13% depending on the climatic and geographical conditions.

Fungi belonging to this genus were isolated on winter wheat plants starting from the germination stage and through to the stage of full grain ripeness. At the tillering stage their share among other pathogens varied between 0.5-16% and at the grain filling – 17.5-38.5% depending on the year conditions. The *Rhizoctonia* fungi, causing root rot on winter wheat, include several species: *Rhizoctonia solani* Kuhn. Teleomorph - *Thanatephorus cucumeris (A. B. Frank)* Donk, *Rhizoctonia cerealis* Van der Hoeven. Teleomorph - *Ceratobasidium cereale* D. Murray & L. L. Burpee *(*Anastomosis – *AG-D.) u Rhizoctonia oryzae* Teleomorph - *Waitea circinata* var *oryzae (*Anastomosis WAG-0*); Rhizoctonia zeae* Teleomorph - *Waitea circinata* var. *zeae (*Anastomosis WAG-Z*),* and *p. Gaeumannomyces - G. gramynis* var *tritici, G.graminis* var *avenae u G. gramynis* var *graminis.*

Root rot causing fungi belonging to *Gaeumannomyces* genus are widely presented in the Western Sis-Caucasia. They can cause root rot, foot rot or mixed type rot disease on winter wheat. We have observed that the pathogen better survives in dry summers. We have isolated *G. gramynis* var *tritici, G.graminis* var *avenae and G. gramynis* var *graminis* on winter wheat growing in the Western Sis-Caucasia. Although, their occurance and frequency flactuated depending on the year conditions, location and even preveious crop.

We have isolated various strains of these fungi and examined their pathogenicity to 35 varities developed in Krasnodar, Odessa and Zernograd. Resistant varieties have not been detected.

Currently, we continue studying biological properties of *Rhizoctonia* and *Gaeumannomyces* fungi, as well as the necessity and availability of means to control root rot on winter wheat.

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INNOVATION PROJECTS PARTICIPANTS' WORKING PARTNERSHIP ADMINISTRATION

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High risk and high cost innovation projects, as a rule, is carried out by several participants. In this connection the investors need to have a model of the future coordination of the participants' behavior within the framework of the project, where the contract relationships are reflected in. The contract drawn between the innovation project participants allows the sides not only to organize their activity in the best way during a prolonged period, but also is a condition for using its performance different defence mechanisms coming to the corresponding partner's constraint to fulfill the contracted liabilities.

The contract crude structure being a model of the teamwork consists of two parts:

1.The activity desired parameters description. Within this part the sides negotiate the following points of their contribution towards the innovation project:

- Investment outlay;
- Current production expenditures;
- Educt distribution.

2.The description of the mechanism of the desired results distributions and their interactions. In the given part of the contract the sides negotiates the forms, sizes and terms of the beginning of the participants' responsibility for their obligations violation. At that, risk events can also be classified according the following three moments: investment outlay, current production expenditures and educt distribution.

Considering the realization variants of the innovation project on creation of new product line samples in terms of a scenary approach the following variants of the projects' development have been detached:

1.A new product development is financed by an enterprise individually; all the rights to the construction documentation belong to the consumer after its being paid.

2.The consumer and performer cofinance the project; however, all the rights belong to the consumer on the payment results.

3. The consumer and performer cofinance the project and are joint proprietors of the rights to its results. The development contractor gets a fixed profit margin from the realization of the output produced according to the worked out by him construction documentation.

4.The consumer and performer cofinance the project and are joint proprietors of the rights to its results. The development contractor gets a fixed percentage of the profit.

In every of the mentioned above cases the innovation project participants consider: the conditions of investment and current project finance, the desired results: the profit margin got by every side and the ownership of the work results.

Let us notice, that every variant from the mentioned above ones of the project development can be significantly expanded, when taking into account the time aspect: nonrecurrent or stagewise investment project finance, single or time-consuming getting results from the project implementation.

Thus, taking into account a long term character of innovation projects and multivariance of their realization, the major task for their participants is the consideration of all possible conditions for the project implementation and the choice of the most effective one both for all the participants as a whole and every one individually.

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INNOVATIVE STRATEGY IN ASPECT OF PERSPECTIV ECONOMICAL INTERESTS

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Necessity of innovative strategy is caused by satisfaction of perspective needs of a society as a whole and necessity of maintenance of macroeconomic balance and proportions of economic system in reproduction aspect with long-term prospect. In turn, effective innovative strategy of the state forms economic policy with its components: a structural, budgetary-tax, monetary and credit, social, external economic policy, etc., and also conditions for effective activity of subjects of managing, promotes their integration by means of the coordination of current and perspective economic interests of subjects of market attitudes.

In this case political-economical research of a problem lays in a plane of the analysis of mechanisms of the coordination of interests during development and realization of effective innovative strategy, realization of current and perspective interests by means of economic policy, and also a substantiation of necessity of perfection of these mechanisms.

At such statement of a problem naturally there is a question on maintenance of opportunities and

conditions for the adequate coordination of current and perspective interests during development of innovative strategy, a choice of its basic directions. The effective economic mechanism is the base defining opportunities and productivity of formation of effective strategy in conditions of the market, in particular, by means of stimulation and motivation.

Despite of available contradictions of economic growth and the developed disproportions, in Russia there is a potential which is necessary for using effectively. In this connection overcoming of negative tendencies in economy and social sphere, can be provided on the basis of creation of conditions of economic growth adequate to a situation on the basis of perspective interests of subjects of economy in aspect of development of innovative economy.

In that case translation of economy in qualitatively other condition will allow on the basis of economic growth and innovative making to overcome system deformation reproduction cycles, all levels that will render return influence on formation of favorable conditions of economic growth in the long term and preservation of quality of an environment.

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ENVIRONMENTAL ECONOMICS IN TERMS OF ADVANCED ECONOMIC INTERESTS

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The acuteness and complexity of ecological-economical problems in conditions of advanced exchange relations formation in domestic economy conditioned the necessity of management development priority orientations working out in terms of advanced economic interests of economic agents. As far as the economic intercourse and interests system comprises all public production phases and spheres, specifically manifesting in every of them, in particular, in the sphere of management, in this connection the strategic management supposes the working-out of economic strategy, which includes the coordination and realization of economic interests of exchange relations subjects in all hierarchic management levels leading to the quality economic growth achievement as one of the most important conditions of sustainable society development. Such a necessity is defined by the place of the interests in the economy mechanism, by their role in formation and realization of economic strategy, in the course of development and performance of which it is necessary to take into account and define the ways of coordination and realization of the current and, especially, advanced interests of economic agents.

The environmental aspect is becoming the one of the current interest in present-day economic environment. In the world's practice the strategic point is taken by the structural economic adjustment stimulation on the basis of maintenance of environment, ecological balance support, when, together with production potential modernization of traditional branches most recent branches rapid growth inclusive of economic agents' advanced interests is motivated for sustainable ecological production.

In connection with this, the negative trends overcoming in economics and social sphere, and also the ecological balance maintenance, can be guaranteed on the ground of creation adequate to the situation conditions of economic growth on the basis of advanced interests of economic agents in the perspective of environmental economics development. In this case, the conversion of the economics into a qualitatively other state will let, on the basis of economic growth and ecological aspect, overcome the all levels reproduction cycles systemic changes, that will render an adverse effect on the formation of cleared conditions of perspective economic growth and maintenance of environmental quality.

In this connection the consideration of present-day environmental economics approaches, strategies and methods for taking environmentally sound managerial decisions and providing a sustained development in the longer term becomes of current interest.

It is necessary to introduce modern methods and mechanisms of sustained development principles realization into science and practice; the emphasis should be made on the problems of social, and particularly, economical and natural sciences integration.

The ecological-economical systems soundness problems are becoming topical as a result of business functions of economic agents in the longer term, such as biological diversity decrease, sensibilities of the human being in front of global changes including climate reversal, problems of natural resources use (water, land, forest, useful minerals, recreational resources, and others) in all geographical latitudes and institutional levels.

In the age of economics globalization, the consideration of the international, national and multidisciplinary aspects while working out the economic growth, economic growth quality maintenance and environmental conservation strategies will help solve the existing problems, bridging over geographical boundaries and the bounds of science disciplines as well.

Special attention should be paid to international and regional ecological-and-economical problems, the development of advanced methodological approaches of environmental economics, problems of harmonization of business interests and maintenance of environmental quality, interaction of all the concerned

(employers, control and environmental bodies, human population, society and others) in the context of sustained development, and also the role of information technologies and modeling in ecological-and-economical management in terms of advanced economic interests.

In this respect the formation of developed exchange relations in Russian economics is largely associated with the solution of the efficient management problem by environmental economics transformations in the aspect of coordination and realization of its agents' interests in the long term.

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THE ANALYSIS OF RESULTS OF MONITORING OF QUALITY WATERS OF PERM CITY WATER ABSTRACTIONS

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Providing the population of Russia with drinking water is one of the priority problems to solve for health protection, better working conditions, and higher living standard. It has been a spike of ecological catastrophes lately in this country, obstructing reliable and quality uninterrupted water supply (Khabarovsk, Saratov, etc.). This unfavourable situation can be explained by used water supply systems, which have been in operation since the time of the Soviet Union without sufficient investment into support and development; it is also due to the fact that operators and municipalities have been paid little attention to the issues of providing quality life support.

The City of Perm is a regional center with a population of 1,000,000 people consuming 420,000 m^3 of drinking water daily. What is significant for water supply in Perm is that water is abstracted from several artificial surface sources or water reservoirs. The water for the city supply is treated at three water treatment plants: Chusovskaja, Bolshekamskaja and Kirovskaja.

A criterion of any harmful chemical substance level is its maximum allowable concentration or MAC; in case of its violation water is not suitable for one or more applications in terms of water use. Water quality has been determined according to the fish industry standards.

For the raw water quality analysis we have used the data of FGU Kamvodexpluatatsiya, a federal agency providing water quality control in the water abstraction areas. The chemical composition of water has been evaluated on the basis of extreme values of the chemical elements for the years 2003-2006. Water sampling was performed against the water abstractions along the navigation pass of the water reservoirs.

The water of the Chusovaya, Bolshekamsky, and Kirovsky Water Abstractions (WA) differs in terms of mineralization and basic ion content as follows:

1. Water specific conductance (σ) of the Chusovaya WA is within 200-500 μS/cm in the filling period, 300-650 μS/cm during summer-autumn level stabilization, and 250-700 μS/cm (maximum level) during winter drawdown. At the Bolshekamsky and Kirovsky WAs the values are 90-120, 250-500, and 450-700 μS/cm, respectively.
2. The solid residual is higher at the Chusovaya WA during spring and summer (up to 0.5 MAC) with 0.3 MAC at the Votkinskoye Reservoir WAs. In winter the water amount is low resulting in larger solid residual up to 0.6 MAC at the Chusovaya and Bolshekamsky WAs and 0.9 MAC at the Kirovsky WA.
3. The level of hydrocarbonates (HCO3-) is different depending on the water content periods and defined by natural factors. The ion level at the Chusovaya WA is 50-140 mg/l with a maximum value of 170 mg/l during winter drawdown. Downstream of the Kama power plant dam this value lowers to 10-40 mg/l during the filling period, goes up to 20-100 mg/l during water level stabilization, and reaches its maximum in winter low water (60-140 mg/l).
4. The WA sulphate level is similar to the one of hydrocarbonates: minimum in spring – 50-170 mg/l at the Chusovaya WA, 20-30 mg/l at the Bolshekamsky WA, and 20-50 mg/l at the Kirovsky WA; SO42- is higher during the summer-autumn period – up to 70-400 mg/l, 10-100 mg/l, and 40-130 mg/l, respectively; maximum SO42- level in winter – 50-180 mg/l upstream of the town and 60-120 mg/l in the town. The sulphates are above the MAC values at all WAs during the summer-autumn and winter periods. The Chusovaya River natural background with high level of the SO42- ions causes high concentration of the element during the spring filling at the Chusovaya WA.
5. Most chlorides come from the waters of the Kama Reservoir and industrial wastewater of Perm City. The chloride is the main component of the water reservoir chemistry in winter. In spring the level of chlorides is low (5-10 mg/l); during the summer-autumn period it goes up to 10-50 mg/l at the Chusovaya WA and up to 5-20 and 20-70 mg/l at the Bolshekamsky and Kirovsky WAs, respectively. The maximum level of chlorine ions has been noted in winter – up to 80 mg/l at the Chusovaya WA and up to 200 mg/l within the boundaries of Perm City.
6. The Kama Reservoir water has a low content of calcium, which does not exceed the MAC value. In spring Ca2+ has a minimum level of up to 30 mg/l at the Chusovaya WA and up to 70 mg/l at the Bolshe-

kamsky and Kirovsky WAs. During the summer-autumn period it rises up to 90 and 60 mg/l, respectively.

7. It reaches its maximum during winter drawdown – 40-120 mg/l at the Chusovaya WA and 50-90 mg/l at the Bolshekamsky and Kirovsky WAs.

The biogenic matter level varies significantly as follows:

1. In different seasons at the Perm WAs the concentration of ammonium nitrogen ranges from 0.1 to 3.5 MAC. At the Chusovaya WA it reaches its maximum of 1.5 MAC during winter drawdown when the water volume is the least. During other seasons the content can vary within 0.1-1.0 MAC. The water mass in the Votkinskoye Reservoir is greatly influenced by industrial contaminants. During the filling period the NH4+ MAC value is 1.3-2.4 at the Bolshekamsky WA and 1.6-3.6 at the Kirovsky WA, which is also connected with the Kama water drawdown and a low water level in the Votkinskoye Reservoir. During stabilization of the water level the nitrogen content does not exceed the MAC value. The winter drawdown period is unfavourable, since the NH4+ level is within 1.4-2.9 MAC.

2. The level of other biogenic substances – NO2-, NO3-, and P – is within 0.0- 0.3 MAC. Any specific reduction/grow trends along the WAs or in different seasons have been not traced.

The levels of most microelements described constitute a hydrological risk for the water users by reason of high concentrations and violation of the MAC values.

1. Fe varies within 0-12 MAC. During the filling period it grows from 2.0 at the Chusovaya WA up to 7.0 at the Kirovsky WA. A similar picture can be observed during the stabilization period: growth from 1.0 to 5.0 MAC. The highest level is typical for the winter period with 12 MAC at the Chusovaya WA down to 3-7 MAC at the Kirovsky WA.

2. Cu is also much higher than the MAC value (Figure 2): from 10 MAC at the Chusovaya WA to 24 MAC at the Kirovsky WA in spring; 26 MAC at the Bolshekamsky WA and 10-11 MAC at the other WAs in summer and autumn. In winter its concentration grows up to 18 MAC at the Chusovaya WA and 27-25 MAC at the Bolshekamsky and Kirovsky WAs.

3. During the spring filling period the level of manganese grows along the WA sites from 0-5 MAC at the Chusovaya WA up to 5-13 at the Kirovsky WA. (Figure 2). In summer it is 1-6 and 3-18 MAC, respectively. During the low water stand the Mn concentration varies significantly from 7-18 MAC at the first WA, to 12-33 MAC at the second WA, and up to 5-37 MAC at the third WA. It highly depends on operation of local factories. During winter drawdown the Mn level in the basin water reaches its maximum, for the water dilution process slows down significantly.

4. Pb belongs to heavy microelements and has a negative impact on living organisms. Observations have shown its low level, not exceeding the MAC value (up to 0.1 MAC), with one exception of a higher concentration at the Bolshekamsky WA during the navigation period due to water vessels (up to 0.5 MAC in spring and 1.0 MAC in summer).

The gas conditions generally define the evaluation of biota in reservoirs. The oxygen conditions are formed under the influence of a series of positive (wind-and-water-induced mixing, flowage, etc.) and negative (industrial contamination, water bloom, etc.) factors. Their interaction determines favourable water saturation with oxygen during the open channel period (8-10 mg/l in spring, 9-11 mg/l in summer and autumn) and its significant shortage during freeze-up (4-7 mg/l). The worse conditions are in the areas of industrial pollution. At the Chusovaya WA the oxygen level is within 0.5-0.9 MAC with minimum values in winter. The city impact is noted at the Bolshekamsky and Kirovsky WAs: 0.6-0.7 MAC during the reservoir filling period, 0.5-1.2 MAC in summer and autumn (especially when bacteria and algae are most active), and 0.5-1.3 MAC in winter.

The following is typical for the Perm WAs:

1. High element content when the water level is close to the lowest operating one. Such conditions are typical for late winter right before ice movement, as well as for the beginning of filling the reservoir in spring.

2. Among the biogenic elements, exceeding MAC is typical for NH4+ in all water regime phases, especially in spring (up to 3.6 MAC) and winter (2.9 MAC). This situation is determined by a low water mass volume of the reservoir resulting in poor self-cleaning ability.

3. The level of all elements significantly exceeds MAC, especially during the winter drawdown period.

4. The level of dissolved oxygen in the reservoir is low both in winter (while freezing up) and in summer (during algae bloom), i.e. 4.6 and 5.0 mg/dm3 or 1.3 and 1.2 MAC, respectively. At the same time the BOD and COD are up to 1.9 and 2.6 MAC, respectively.

The percentage of non-standard samples taken from the drinking water sources in Perm is 40% in terms of the sanitary and chemical performance and 15% as for microbiological parameters.

The main risk is connected with the water supply organisational plan. The major city WAs, the Bolshekamsky and Chusovaya, are located on the left bank of the Kama Reservoir, while the right-side water supply is provided through the inverted siphon laid on the bottom of the reservoir. Currently, water is supplied to the right bank through a single line with the other one under rehabilitation. So the water supply is not reliable enough. Moreover, life of the Bolshekamsky water works supplying water to the down town has almost run out for highly deteriorated and obsolete equipment.

Any local measures would not help. The best solution is total system rearrangement providing two independent water supply systems on the right and left banks of the river.

Drinking water supply through the river is to be eliminated due to construction of a new right-bank water treatment plant in the Kama Reservoir water pool. The inverted siphon will be used as an emergency crossover between two separate water supplies located on different river banks. The obsolete Kirovsky and Bolshekamsky WAs are supposed to be abandoned.

On the one hand, such measures will allow avoiding the above situations and, on the other hand, they will improve the quality of water supplied to the system, for construction of a new treatment plant will enable to use up-to-date and effective methods of water treatment.

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ECOLOGICAL ENVIRONMENT AND HEALTH OF THE POPULATION OF THE REPUBLIC OF KAZAKHSTAN

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The purpose of research. To estimate possible influence of the toxic substances acting in an environment as a result of activity of the enterprises of oil-and-gas branch, on a state of health of the population in the Republic of Kazakhstan.

Object and subject of research. As modeling regions the basic oil and gas extraction areas of the Republic are chosen: Mangistauskay and Atirauskay in which territory 188 oil fields and gas or 81.7% of the deposits revealed in the Republic of Kazakhstan are located.

During the work the resource security of public health services and the basic parameters of health state of the population carried out: the demographic situation, including the analysis of number and structure of the population (1996-2005) is determined; primary and total morbidity of the population: on classes of illnesses of the whole population, adults and children. Groups: adults and children - covers 93.8% of the whole population of the Republic.

Mangistauskay oblast on primary diseases of the whole population and adults takes first place in the Republic, and Atirauskay oblast which has as well as Mangistauskay oblast a plenty of oil-and-gas deposits, the last - 14 place on all investigated groups of the population. Taking into account high morbidity of Mangistauskay oblast population the basic researches carried out in this area.

The sanitary condition of water, atmospheric air, maintenance of the population with good-quality food, epidemiological conditions are also investigated.

Methods of research. The analysis was carried out by a method of quantitative measurement of effects of environment influence on health of the population, a method of codification, by an estimation of risk for health of environment factors and its management.

Results of research and discussion. Atirauskay oblast population estimates 472.4 thousand person (3.1% from the Republic population), and Mangistauskay oblast – 374.4 thousand person (2.5% from the Republic population). Atirauskay oblast urban population was equal - to 269.1 thousand person (57.0%), Mangistauskay oblast - to 263.06 thousand person (70.2%), and rural - 203.3 and 111.4 thousand person accordingly (43.0% and 29.8%). Mangistauskay oblast, undoubtedly, concerns to industrial regions as three quarters of its population live in cities, in the Republic the urban population estimates - 57.1%.

In structure of the population of oblasts the number of adults is less, than in the Republic (64.5% in Atirauskay, 63.4% in Mangistauskay and 69.7% in the Republic), and the number of children is more than 28.6%; 30.1% and 24.2% accordingly) at equal relative quantity of women in fertile age in oblasts and the Republic (28.3%, 28.3% and 28.5%). This fact, can be connected, with higher common factor of fruitfulness in oblasts - 1.00 and 1.06; in the Republic - 0.85.

In Atirauskay oblast from 1996 to 2005 the population has increased for 8.5%, in Mangistauskay oblast on 11.2%, and in the Republic during this period the amount of inhabitants has decreased for 5.3%. Obviousiy one of the reasons of population increasing in oblasts is the process of immigration or installation of the population in oblasts. There was a positive balance of migration (the number of coming and leaving): 288 person in Atirauskay oblast and 3730 person in Mangistauskay.

The system of public health services in Mangistauskay and Atirauskay oblasts has typical structure. The Security of the population of oblasts material resources of public health services for 11 years, basically, corresponds or exceeds middle republic level (Charges on 1 inhabitant in one year, scheduled capacity of the polyclinic organizations, security of the population with beds). Security of the population of modeling oblasts with the staff of medical workers is lower than middle republic level.

Atirauskay oblast and Mangistauskay oblast have higher level of birth rate, a natural increase and a low death rate in comparison with republic (progressing demographic structure) that is caused by social factors i.e. the advanced infrastructure of the industry including oil and gas extraction and a high average level of wages: in Atirauskay oblast - 415 dollars, in Mangistauskay oblast - 400 dollars; at middle republic

level - 219 dollars. Expected life at a birth of the population of both areas does not differ from middle republic level and makes about 66 years (In Russia - 64.9 years).

For 11 years the parameter of infantile death rate in Mangistauskay oblast remained at high level and has made in 2005 – 17.4 at middle republic level – 15.2. For comparison: in 2003 the given parameter in Russia made 12.4; in Uzbekistan 16.6; on the average across the CIS - 14.5 on 1000 person born alive.

The conducting reason of death rate of newborns is high incapability of fruit reserving, the number died prematurely born in 2005 has made 126.8 on 1000 person born alive, on republic - 73.7-83.1. The analysis of a parameter of infantile death rate in Mangistauskay oblast for 5 months 2005 has revealed, that - the parameter of infantile death rate is lower than that in the basic oil and gas extraction region of area territories Zhana Ozen (13.5 on 1000 born alive and 14.2 accordingly). At the same, Karakijansky area where Zhana Ozen is located, has the highest level of infantile death rate in oblasts - 24.4. Thus, influence of oil and gas extraction branch in formation of a parameter of infantile death rate is debatable and demands the further scientific verification.

The parameter of mother death rate in 2005г. in Mangistauskay oblast is one of the highest in the Republic and makes 59.7, in Atirauskay oblast – 93.4, in the Republic – 40.5 on 100 thousand born alive, that, is probably connected with the environmentally poor - easing of an women organism and with organizational - not sufficient security of the population of oblasts by doctors of the whole specialities 31.7 on Mangistauskay oblast, 30.1 - on Atirauskay oblast and 36.5 on the Republic on 10000 person of the population), doctors obstetricians-gynecologists on Mangistauskay oblast – 2.6, on Atirauskay oblast 2.1 (on the Republic - 2.7 on 10000 person of the population) and not duly receipt of pregnant women under supervision of female consultation (till 12 weeks of 68.6% in Mangistauskay oblast, 55.1% in Atirauskay oblast and on the Republic of 71.7%.

In the Republic in 90th years the regressing structure of the population took place: birth rate and a natural increase decrease, the parameter of death rate annually increased. The character of change of infantile death rate had a negative orientation. Since 2002, the demographic situation in republic was stabilized

Primary morbidity of population Atirauskay oblast are lower than average on the Republic. On Mangistauskay oblast the highest primary morbidity of the population takes place during the analyzed period (1995-2005гг).

The first place in structure of primary morbidity of the population of oblasts and the Republic in 2005г. is taken by illnesses of system of breath. Determining factor in formation of this group of a pathology is allocated to a condition of atmospheric air. In Mangistauskay oblast this pathology makes 30.7%, in the Republic - 39.4% that does not allow to assume causal conditionality of these diseases by oil and gas extraction branch functioning in area.

The second range in structure of diseases of the population of oblast taken by illnesses of digestion system (9.8 %), on the Republic - by illnesses of urinogenital system (7.5%).

It is not excluded, that one of the reasons of defeat of a gastroenteric path of population in Mangistauskay oblast is its low security with good-quality potable water. 70.0 % of the population of rural territories of oblast are provided with imported potable water pipe, use water only 12.0 % of the population; use columns - 4.0 %; wells - 12.0%. Unsatisfactory security of food is marked in oblast, in comparison with 1990 consumption of meat and meat products has decreased as well as manufacture of milk and dairy products from 11.9 thousand tons up to 0.2 thousand tons has decreased. Manufacture of sausages, groats has completely stopped. There is no manufacture of oil creamy, vegetables, sugar. Monotonous, basically carbohydrate, meal results in functionalities easing of an organism of adults and children, backlogs children growth and development. An insufficient and unbalanced meal results anemias at women of the fertile period, frequently meeting in regions, that, in turn, can be one of the significant reasons of high infantile death rate in perinatal period.

The third place in 2005 in structure of diseases of the population of oblast illnesses of an eye - (7.6%), as body, carrying out the first contact to an environment, on the Republic - traumas, poisonings and some other consequences of influence of the external reasons (7.2 %).

In structure of primary morbidity of adult population in Mangistauskay oblast neoplasms has a level below then middle republic level, that excludes causal conditionality of these diseases by oil and gas extraction branch functioning in area. More vulnerable children's population has higher level of neoplasms, than on the Republic. However, connections of a level of children neoplasms with staing in territories of oil and gas extraction it is not traced.

The high level of primary morbidity of the whole population and children Mangistauskay oblast by illnesses of blood and congenital anomalies estimated. The number of the congenital anomalies not compatible with a life being the reason of infantile death rate, on oblast is less, than on the Republic. High primary morbidity of population Mangistauskay oblast can be a result of good revelation of diseases. The active treatment, competent primary and secondary preventative measures decrease invalidization and the death rate.

The statistical analysis has revealed presence of positive correlation of different forces of primary morbidity of the whole population by all illnesses and of breath system and emissions of substances pollut-

ing of an atmosphere in Mangistauskay oblast and the Republic of Kazakhstan.

Taking into account, that this connection is characterized as strong for the Republic of Kazakhstan and weak for Mangistauskay oblast, it is possible to conclude, that negative ecological influences of oil and gas extraction branch on population health corrects high level wages, allowing to provide the population with more physiologic feed and to raise availability of medical aid.

Conclusions:

1. Progressing demographic structure of Atyrauskay and Mangistauskay oblasts in last decade is characterized by high birth rate, a natural increase, the common factor of fruitfulness at a low death rate of the population, in oblast growth of average life expectancy that is caused by the advanced infrastructure of the industry, including oil and gas extraction, and is registered by a high level of wages of the working population.

2. The system of public health services in Atyrauskay and Mangistauskay oblasts has typical structure. Security of the population of oblasts material resources of public health services for 11 years, basically, corresponds or exceeds middle republic level. It is established by unsaticfacted number of a staff of medical workers in modeling oblasts.

3. The state of population health in Mangistauskay oblast characterized by the highest, and in Atyrauskay oblast by the lowest level in the Republic of primary morbidity of the whole population by all illnesses. The structure of primary morbidity of population of Mangistauskay oblast differs from structure of primary morbidity of the population in the Republic of Kazakhstan. Low death rate of population in Mangistauskay oblast in comparison with the population of the Republic testifies to the best detectability of diseases and a high level of preventive and medical activity of public health system.

4. The statistical analysis of the oil and gas extraction enterprises on health of the population of the Republic of Kazakhstan allows to conclude, that possible negative ecological influences of oil and gas extraction branch on health of the population better a high social standard of living of the population of regions.

Recommendations. Carrying out of the further profound complex medical-demographic researches of a health state of the population of oil and gas extraction regions under the special program is necessary in view of morbidity and death rate according to age and professional groups.

The decision of questions of material stimulation of work of medical workers will allow to solve questions of security of the population of oil and gas extraction areas with doctors - obstetrician - gynecologists and to lower mother and infantile death rate.

Controls public health services in Atyrauskay and Mangistauskay oblasts can recommend introduction and perfection of activity obstetric-therapeutic-pediatric complexes, as optimal form of work on improvement of the children's and female population of area.

The constant control of sanitation and epidemiological quality of air, potable water in areas and food is demanded. The increase in financing of construction and reconstruction of water pipes will positively reflected in an epidemiological situation in area.

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NEW ENVIRONMENTALLY SAFE PLANT ADDITIVES FOR MEAT PRODUCTS MANUFACTURING APPLICATION

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At the heart of Russian food consumers' preferences traditionally there are two criteria – customs and food price. But recently a third criterion has got a greater occurrence: it is quality. This is a distinctive feature of the new food market, this is the appearance of choice, this is the sign of the fact that our producers have become interested in the consumers' preferences. The food products quality is made of many characteristics. The notion "quality" includes the conformity with the branch accepted standards, chemical constitution, biologic and energy value, biological effectiveness, ecological safety, technologies' and ultimate product's safety, equivalence of the product's composition to the human body's needs depending on the form of activity, health status, age, sex, physiological features – pregnancy, baby feeding, advanced physical or mental work load, etc.

The food-processing industry current trends stimulate the ordered composition food production planning. It is caused by the fact that no one natural commodity contains all necessary for the body substances in the amounts providing its physiological needs. One of the ways to correct the chemical constitution of meat products is using biologically active substance rich medicinal herbs in production. The formulation of meat raw stuff functional products of prophylactic and bracing properties enables the regulating for preventive and therapeutic purposes' sake finely and complexly. The influence of crude drug on forcemeat properties has been investigated incompletely. In connection with the above said the following problems were set by us: to study the biochemistry of medicinal plants growing in the Oryol Region territory, to evaluate physical-chemical and functional-processing behaviour of meat raw stuff and their application. While selecting the plant materials we were ruled by the availability and popularity of them in the

region for the provision of storage (State National Nature Reserve "Oryol Polesye"). We chose Greek-valerian polemonium and purple coneflower growing in its territory.

According to the obtained experimental findings the investigated medicinal plants are characterized by a high protein content. The hard core of it consists of freely soluble albumens and globulins. It is of great importance as albumens and globulins are regarded as high-functional components which together with muscle proteins stabilize the proteinaceous matrix of meat systems. Besides, the leaves and seeds contained much iron, that will allow increasing the hemoglobulin level in the consumers while using the given plant raw material products.

The proteins electrophoresis showed that the most saturated material according to electrophoretically mobile albumen and globulin proteins is the one obtained from the purple coneflower.

Taking into account the experimental study data is possible to suppose that the plant raw material from the Greek-valerian polemonium and purple coneflower is rich in functional proteins and is fortified with ash constituents, especially iron salts.

The use of water infusions of the investigated plants can promote the formation of taste-and-smell characteristics and the directed regulating of such technological processes as secondary structure formation, dehydration and selective flora cultivation. The application of the denoted medicinal plants in the meat industry will promote enriching meat products with biologically active substances. In the future the concentration assortment and the balance of meat and plant raw materials for comminuted meat products will be carried out.

An individual of a modern urban society is fated to some or other food failures, and with that he always will be attended with the corresponding body defence systems' inability to response adequately to environmental nuisances, that suddenly increases the risk of many medical conditions development.

The population nutrition problem can be solved by means of creation of a given chemical composition meat-and-plant products wide range. The highest point of this direction can be therapeutic and functional food products, and also the product's biosafety guaranteeing.

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PRESENT TIME: CRITERIA AND EXISTENCE POSSIBILITY

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The article is dedicated to the problem of determination of criteria of the present. The authors project and prove the idea: the duration is defined only in the moments of its interruption, as the time essence is in the dialectics of the continuity interruption. The present is limited by two interruptions and starts being perceived as a fractal – infinitely divisible moment. The comprehension of time as "the other side" of information is substantiated.

The affirmation about three time modes: past, present and future, is an exoteric one. The difference between them is, according the dynamic time concept, in the fact that there is no future yet, and there is no past already. But relative to the present moment the events continuously change their position: the future events are transformed into the events of the present, and the present events – into the events of the past. Thus, the affirmation about the reality of the present infers from it. But whereupon does our confidence that the present really exists rest on? Indeed, any act of consciousness about the present takes place in relation to the one that has already happened, and hence, to gone to the past. The endless "glissade" to the past is overcome only in the consciousness which neglects this constant loss of the present moment and equipoises this backward movement by the aiming at the future, forwards.

Of course, it is possible to take for the "instant of time" a certain time interval (which, in its turn, is determined by the duration of a certain event): a second, a month, even a cosmic year – then, with a clear conscience, one can make a statement of the type: "at the present moment, which has been lasting since 1908, the following events took place…" The poorness of such an equation of the essence (of the present) to the present state, event, i.e. to the phenomenon level, is evident. However, it is it that one had to be satisfied with. Contrary to such an approach one is forced to accept the fact that we have no criterion for choice of the present, which was paid attention to by Mc-Taggart in the above mentioned 1908 [1].

Really, to connect the present with the availability means to run into a plain contradiction, for just the availability is constantly open to question. We can reason about traces of real events, which remain in our consciousness, but the events themselves, alas, escape migrating to another mode of time. Even if we proceed from the premise that a real event and the trace that it leaves are simultaneous (that needs to be proved as well), anyway the event and its time are different things at all. What do we measure the duration (as the very first availability indicator of time) with? Only with the moments of its interruption we can fix the beginning and the end of any qualitative continuity and it is measuring of this section that allows us to speak about the duration. As an illustration of the dialectics of interruption of continuity as the time essence let us recollect a well-known tale about Cinderella. Cinderella ran away from the ball so fast that she lost her crystal shoe. It *had* just *been* on the foot, then it *was* away from the foot, and then there appeared this crystal shoe on her foot in *the moment,* which was defined by the event: Prince found her. Between these events ("had been on the foot", "was lost" and "is again on the foot") *no* one other event of *the same range* happened to Cinderella, though many other things missing this range took place. In other words, between the events "had been on the foot" and "is again on the foot" there *was nothing*. And this very "*nothing*" is the present, relative to which the events flow from the future to the past. Thus, there is the present where there is no time: it is interrupted. The present is limited by two interruptions and it itself starts being perceived as a fractal – infinitely divisible moment. Herein the "paradox of the present" is contained: the present exists (for there is something, for which it is the measure of changing and mea-

suring) and it doesn't exist (for it aspires to "slip" out of the reality of the present into the past).

Therefore, we come to the necessity of considering the interrelationship between time and information. In the very general concept information can be defined as a special form of reproduction, conversion, preservation and utilization of the structure and peculiarities of one system into another. In information, first of all, the structure of that very content, which is transferred, stands out. This structure is spatial and temporal. Getting nothing from the physical nature of the source, without reproducing immediately the physical nature of its elements, information "bears" in itself the source's structure (and through it – the content) to the addressee. It is of crucial importance, that the role of information is played not by the source's structure taken by itself, but the reproduction of it in the addressee. Between the source's structure and its reproduction in the addressee there is the same interruption that is between the present and the other two modes of time. Information lies in the ability of a given system to reproduce, preserve and utilize the structure /and "encode" the content/ of another system. It is necessary to distinguish between the following two sides of information: 1/ information as the ability, the property of a definite system class to reproduce, preserve and utilize the structure /and encode the peculiarities, the content through it/ of other systems; and 2/ information as the source's "model", as its image. Information as the source's "model" and information as the ability to accept the "model" – these are the two sides of one and the same phenomenon. If information is the transfer, the reflection of diversity in any objects and systems /of non-animated and animated nature/, then it is time that is the other side of information. Time expresses the dynamics of content, series of changes in subsistence, procedureness and existence becoming, violation of its limits.

The theme of time clearly reechoes with the theme "information" because every change in the acquiring information system is based on some series of states, their duration, rhythmics, etc. Already N. Winter noted that information is a measure of organization, and time – is an inner method of organization through frequency, duration, rhythm, etc. Can information and time exist without each other? Information exists in time, and time is changed under the influence of information. Let us imagine a system possessing no information /such a system is hardly possible, because the interaction of the elements composing it already provokes the whole system change; the system constantly receives information from its elements and sends them its signals. We can only abstract away from these inner interdependencies/. Does this system possess time? If really no information exchange takes place in it, therefore there are no changes. That is why there is no time there. But this system is involved into a wider system, in the time of which it exists. If the system receives and accepts a signal /as an information unit/, then it provokes its change. The given change is time. It is possible to say that information "creates" time. For example, neurophysiologists outline the facts testifying that the synapses accepting information from afferents of the first order possess the ability to convert time, and this, in its turn, leads to accentuation or abstraction of the entries' certain new properties. This ability of synapses to receive new information in terms of time transformation is holding much promise for the analysis of time and information interrelationship.

Information is inconceivable without material systems interaction. The penetration of more and more information into a system /no matter outer or inner/ "perturbs" it. And time in this case serves as an organizing and regulating matter. The system will be destroyed, if after receiving some information it makes a try to exist in another rhythm, which is inadequate /incommensurable, incompatible/ to the one, which is comprehensible for it. In the ancient Chinese book "Yi Ching" /"Book of Changes"/ it is said that a careless interference even into a process of a second-

ary importance can lead to irreversible alterations in the world. A negligibly small action can result in significant consequences.

Information is a thing that changes the system perceiving it. But hereby, it changes not only the content, structure, but also the time of the perceiving system. Time can be understood exactly as an organizing structure, isomorphic one for various complexity self-organization processes. Leibniz's idea of reflection of one monad in another is a prerequisite of synchronization idea – one of time properties "working" in the line of systems' self-organization. In the process of interreflection, according Leibniz, the coordination and synchronization of monads take place. The cooperative, coherent states represent the most highly organized form of inanimate matter – that is the word of science, which confirms the old guess expressed by Hegel [2].

Therefore, time plays a triple role of an organizing matter in the information interaction: 1/ the source of information reproduces among its own immanent properties and relations its temporal characteristics; 2/ the information transfer itself – is a process taking place in time; 3/ as the result of receiving information time alterations of the system perceiving it occur.

A system keeps informed about many states: both past and future. During its life the system goes through several bifurcations, where the choice of one of the possible sound branches of the system's further development is carried out. The information about this moment is transferred up to the following bifurcation, and "something born or done in this moment possesses the properties of this moment of time" [3]. The bifurcation points are those interruptions, which separate the present from the past and the future. Time, therefore, is a picture of interruptions, in the moments of which various choices occur.

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