CONTENTS

INFLUENCE OF KETOTIFEN, CROMOLYN SODIUM, AND COMPOUND 48/80 ON THE SURVIVAL RATES AFTER INTESTINAL ISCHEMIA REPERFUSION INJURY IN RATS

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Background: Mast cells were associated with intestinal ischemia-reperfusion injury, the study was to observe the influence of Ketotifen, Cromolyn Sodium (CS), and Compound 48/80 (CP) on the survival rates on the third day after intestinal ischemia-reperfusion injury in rats.

Methods: 120 healthy Sprague-Dawley rats were randomly divided into 5 groups, Sham-operated group (group S), model group (group M), group K, group C and group CP. Intestinal damage was triggered by clamping the superior mesenteric artery for 75 minutes, group K, C, and CP were treated with ketotifen 1 $mg \cdot kg^{-1}$, CS 50 $mg \cdot kg^{-1}$, and CP 0.75 $mg \cdot kg^{-1}$ i.v. at 5 min before reperfusion and once daily for three days following reperfusion respectively. Survival rate in each group was recorded during the three days after reperfusion. All the surviving rats were killed for determining the concentration of serum glutamic-oxaloacetic transaminase (AST), glutamic pyruvic transaminase (ALT), the ratio of AST compare ALT (S/L), total protein (TP), albumin (ALB), globulin (GLB), the ratio of ALB compare GLB (A/G), phosphocreatine kinase (CK), lactatedehydrogenase (LDH), urea nitrogen (BUN) and creatinine (CRE) at the 3rd day after reperfusion. And ultrastructure of IMMC, Chiu's score, lung histology, IMMC counts, the levels of TNF-α, IL-1β, IL-6 and IL-10 of the small intestine were detected at the same time.

Results: Intestinal ischemia-reperfusion injury reduced the survival rate. The concentrations of TP, ALB and level of IL-10 in intestine in group M decreased significantly while the concentrations of S/L, LDH and the levels of IL-6 and TNF-α in intestine increased significantly compared with group S ($P < 0.05$). Treatment with Ketotifen and CS increased the survival rate compared with group M ($P < 0.05$), attenuated the down-regulation or up-regulation of the above index ($P < 0.05$).Treatment with CP decreased the survival rate on the 3rd day after reperfusion compared with group M ($P < 0.05$). Group K and C had better morphology in IMMC in the small intestine and in the lungs than in group M and CP, although the Chiu's score and IMMC counts remained the same in the five groups ($P > 0.05$).

Conclusion: Mast cell inhibition after ischemia prior to reperfusion and following reperfusion may decrease the multi-organ injury induced by intestine ischemia reperfusion, and increase the survival rates.

Background

Intestinal ischemia-reperfusion injury (IIRI) contributes to the pathophysiology of many conditions, including abdominal aortic aneurysm surgery, small bowel transplantation, cardiopulmonary bypass, strangulated hernias, and neonatal necrotizing enterocolitis [1, 2]. In addition to localized tissue damages, IIRI induces inflammatory damages in remote organs, particularly in the lung and liver, and is associated with a high mortality [3].

Intestinal mucosal mast cells (IMMC) are particularly frequent in close proximity to epithelial surfaces, where they are strategically located for optimal interaction with the environment and for their putative functions for host defense [4]. Previous studies demonstrated that the degranulation of IMMC can be induced by oxidants generated in the post-ischemic gut, and the released inflammatory mediators such as histamine and tumor necrosisfactor-α (TNF-α) could aggravate the injury to intestine after reperfusion [5, 6].

Cordeiro and colleagues reported that administration of diphenhydramine (50 mg/kg, H2 blocker) before reperfusion can significantly reduce the extent of flap necrosis and the neutrophil and mast cell counts caused byischemia/reperfusion [7]. Kalia found that all ketotifen-pretreated animals (1 mg/kg orally twice a day for 3 days before ischemia) survived in 12 hours after ischemia-reperfusion (I/R), while the ten untreated animals subjected to intestinal I/R failed to survive the reperfusion period (Each group had 12 animals) [8]. The above results prove that administration of antihistaminic agents could decrease IIRI.

The influence of administration of mast cell membrane stabilizer, H2 blocker or mast cell degranulator on the damage and the survival rate caused by IIRI after intestinal ischemia have not previously been well investigated. The purpose of our present investigation was to observe the influence of Ketotifen, cromolyn sodium, and compound48/80 on the survival after intestinal ischemia-reperfusion injury in rats, and provided a new therapeutic method to treat IIRI.

Methods

Establish the small intestinal ischemia-reperfusion injury model in rats and the experimental design

This study proceeded after being reviewed and approved by the Institutional Animal Care and Use Committee in accordance with the ethical principles provided by the Experimental Animal Laboratory of School of Medicine, SUN Yat-sen University. Forty-eight healthy Sprague-Dawley rats (weighing 200–250 g) were randomly divided into four groups. Each of which contained 12 rats, the group I (the ischemia time was 60 min), group II (the ischemia time was 75 min), group III (the ischemia time was 90 min), and group IV (the ischemia time was 120 min). Laboratory temperature was kept at 25–27°C. Surgery was conducted under general anesthesia with intra-peritoneal sodium pentobarbital (45 mg/kg) after they had been fasted for 18 h. The rats' abdomens were opened and their superior mesenteric artery (SMA) were found and clamped for 60, 75, 90 and 120 min respectively. Then the clamp was released and abdominal membrane, muscle and skin were sutured gradually. In addition, 5%Cefoperazone was injected intra-peritoneal to avoid wound infection. Animals were housed individually in wire-bottomed cages, free to eat water and food. The survival rates in each group were observed during the 1st day to the 7th day after intestine ischemia/reperfusion.

Based on the above result, One hundred and twenty healthy Sprague-Dawley rats (200–250 g) were randomly divided into five groups. Each of which contained 24 rats, Sham-operated group (group S), model group (group M), Ketotifen treated group (group K), cromolyn sodium treated group (group C) and compound 48/80 treated group (group CP). Intestinal damages were induced by clamping the superior mesenteric artery for 75 minutes based on the above study. Group K, C, and CP were treated with ketotifen (Sigma; USA) 1 $mg \cdot kg^{-1}$, CS (ICN; USA)50 $mg \cdot kg^{-1}$, and CP (Sigma; USA) 0.75 $mg \cdot kg^{-1}$ via caudal vein at 5 min before reperfusion, respectively, while group S and M were treated with the same volume of saline. Then the clamp was released and abdominal membrane, muscle and skin were sutured gradually. In addition, 5% Cefoperazone was injected intra-peritoneal to avoid wound infection. Animals were housed individually in wire-bottomed cages, free to eat water and food. The surviving rats in group K, C, and CP were treated with ketotifen 1 $mg \cdot kg^{-1}$, CS 50 $mg \cdot kg^{-1}$, and CP 0.75 $mg \cdot kg^{-1}$ via caudal vein once daily for 3 days after reperfusion respectively, while group S and M were treated with the same volume saline.

Survival rates

The survival rates in each group were observed during the1st day to the 3rd day after intestine ischemia/reperfusion. The state, action, drinking and eating of each surviving rat was also recorded.

Preparation of specimens and measurements

The surviving rats were sacrificed by anesthetic overdose.8 rats in each group except only 3 rats in group CP were paunched rapidly on the 3rd day after reperfusion. 2 mL blood was obtained from the inferior vena cava, frozen at -20°C for 5 minutes and centrifuged for 15 minutes at4, 000 r/min. Supernatants were transferred into fresh tubes for evaluation of concentration of glutamic-oxaloacetic transaminase (AST), glutamic pyruvic transaminase (ALT), the ratio of AST compare ALT (S/L), total protein (TP), albumin (ALB), globulin (GLB), theratio of ALB compare GLB (A/G), phosphocreatine kinase (CK), lactate dehydrogenase (LDH), urea nitrogen (BUN) and creatinine (CRE)

through automatic biochemistry analyzer (abbott, USA).

Intestine histology

A 0.5–1.0 cm intestinal segment was cut 5 cm from the terminal ileum and fixed in 4% formaldehydum polymerisatum, then embedded in paraffin for sectioning. The segment was then stained with hematoxylin-eosin. Damages of intestinal mucosa were evaluated by two different histopathologist according to the criteria of Chiu's method [9]. Criteria of Chiu grading system consists of 5subdivisions according to the changes of villus and gland of intestinal mucosa: grade 0, normal mucosa; grade 1, development of subepithelial Gruenhagen's space at the tip of villus; grade 2, extension of the space with moderate epithelial lifting; grade 3, massive epithelial lifting with a few denuded villi; grade 4, denuded villi with exposed capillaries; and grade 5, disintegration of the lamina propria, ulceration and hemorrhage.

Transmission Electron Microscopy

Another 0.5 cm intestinal segment cut 5 cm from the terminal ileum were immersed and fixed in 2.5% glutaraldehyde overnight at 4°C and washed three times in PBS. They were then post fixed in aqueous 1% OsO_4 and 1%K_3Fe $(CN)_6$ for 1 hour. Following three times of PBS washing, the tissue was dehydrated through a graded series of30 to 100% ethanol and 100% propylene oxide and immersed in 1:1 mixture of propylene oxide and Polybed812 epoxy resin for 1 hour. The infiltration solution was then changed to 100% resin. After 24 hours of infiltration, the tissue was embedded in molds and cured at 37°Covernight, followed by additional hardening at 65°C for2 days. Ultrathin (70 nm) sections were collected on 200-mesh copper grids and stained with 2% uranyl acetate in50% methanol for 10 minutes, followed by 1% lead cit-rate for 7 minutes. Sections were photographed using a Hitachi H-600 transmission electron microscope (TOSHIBA, Japan) at 80 kV onto electron microscope film.

Lung histology

A median sternotomy was performed. The harvested right middle lobe of the lung was fixed in 4% formaldehydeum polymerisatum. Paraffin-embedded sections (5 μm) were stained with hematoxylin-eosin and evaluated blindly by two different histopathologist.

Detection of concentration of protein in intestine

Another segment of 10 cm intestine was cut 5 cm from terminal ileum. The small intestine was washed with frozen saline and dried with suction paper at 4°C. Intestinal tissues were homogenized with normal saline. Intestinal protein (content) was quantified by the Bradford method with a BSA standard kit, provided by Shenerg BiocolorBioScience & Technolgy Company, Shanghai, China.

Detection of the levels of TNF-α, IL-1β, IL-6 and IL-10 in the intestine

Intestinal tissues were homogenized with normal saline, frozen at -20°C for 5 minutes and centrifuged for 15 minutes at 4, 000 r/min. Supernatants were transferred into fresh tubes. The levels of TNF-α, IL-1β, IL-6 and IL-10 were measured using a bead-based immunofluorescence assay (Luminex Inc. Austin, TX, USA) using multiplex cytokine reagents supplied by Linco International, USA. Briefly, antibody-coupled beads were incubated with the samples (antigen), followed by incubation with biotinylated detection antibody and streptavidin-phycoerythrin, respectively. A broad sensitivity range of standards (Linco International), ranging between 1.95 and 32 000 pg/ml were used to help enable the quantization of a dynamic wide range of cytokine concentrations and provide the greatest sensitivity. This captured bead-complexes were then read by the Luminex fluorescent bead-based technology Luminex™ 200 Liquid Array (Luminex Corporation Austin, TX, USA) with a flow-based dual laser detector with real-time digital signal processing to facilitate the analysis of up to 100 different families of colour-coded polystyrene beads and allow multiple measurements of the sample ensuring in the effective quantification of cytokines. The levels of TNF-α, IL-1β, IL-6 and IL-10 in the

intestine were indicated as picogram per milligram of protein.

Immunohistochemical detection of tryptase in intestine

Five-micron-thick sections were prepared from paraffin-embedded intestinal tissues. After deparaffinization, endogenous peroxidase was quenched with 3% H_2O_2 in deionised water for 10 minutes. Nonspecific binding sites were blocked by incubating the sections in 10% normal rabbit serum for 1 hour. The sections were then incubated with polyclonal rat anti-mast cell tryptase (dilution 1: 50)for 30 minutes at 37°C, followed by incubating with biotinylated goat-anti-rat IgG at room temperature for 10–15 minutes. After 3 times rinsing of the sample with PBS for 5 minutes, the horseradish-peroxidase-conjugated streptavidin solution was added and incubated at room temperature for 10–15 minutes. The antibody binding sites were visualized by incubating with diaminobenzidine-H_2O_2 solution. Sections incubated with PBS instead of the primary antibody were used as negative controls. Brownish granules in the cytoplasm were recognized as positive staining for tryptase. We calculated the tryptase positive mast cells in 5 representative areas at 400Ч magnification by Image-Pro Plus 5.0 (USA)

Statistics

Data were expressed as mean ± SD. Analysis of variance was performed using SPSS 11.0 software. One-way analysis of variance was used for multiple comparison. Bonferroni test was used for intra-group comparison or Tamhane's T2 test was used if equal variances was not assumed. Chi-Square test was used to determine the significance of differences of the survival rates. Differences were considered significant when *P* value was less than0.05.

Results

Changes of survival rate after different ischemia time

The 1st to 7th day's survival rates after 60 minutes' intestine ischemia were from 83.3% to 75%. The 1st to the 7th day's survival rates after 75 minutes' intestine ischemia were from 50% to 41.6%. The 1st to 7th day's survival rates after90 minutes' intestine ischemia were from 33.3% to16.7%, while the 1st to 7th day's survival rates after 120minutes' intestine ischemia were from 16.7% to zero. The survival rates on the 3rd day groups I, II, III and group IVwere 83.3%, 41.6%, 25%, and 0, respectively. There were almost no animals died in the 4th to the 7th day after reperfusion. (Fig. 1).

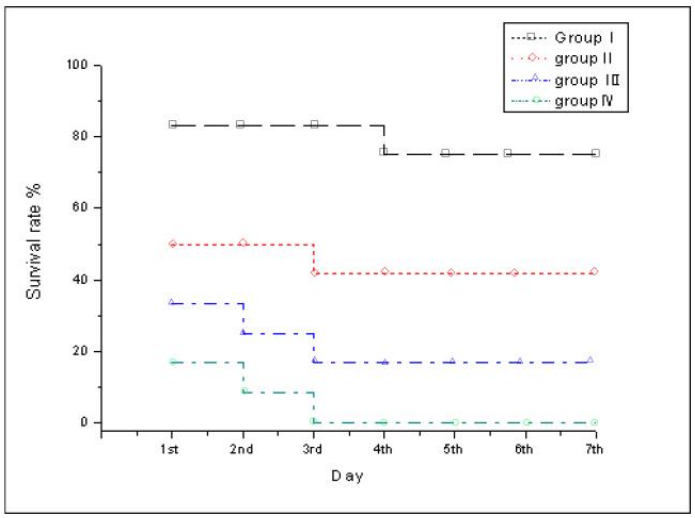

Fig. 1. Changes in survival rate after ischemia and reperfusion injury (establish animal model).

Group I (60 minutes of ischemia), group II (75 minutes of ischemia), group III (90 minutes of ischemia), and group IV (120 mins minute of ischemia).

Changes in survival rates and states after operation

The surviving rats in group S recovered more vigorouslyand vitally on the 3rd day after 75 min intestine ischemia. The survival states of the rats in group M, K and C also recovered vigorously and vitally while those in group CP recovered less vigorously and vitally.

The survival rates in group S were higher than those in the ischemia-reperfusion groups, and the 3rd day's survival rates in group M were lower than those in group K and C while they were higher than those in group CP ($P < 0.05$), there was no significant difference between group K and group C ($P > 0.05$). [3rd day's survival rates: group S92% (22/24), group M 42% (10/24), group K 75% (18/24), group C 75% (18/24), group CP 12.5% (3/24)] (Fig.2)

Changes of serum biochemical indicator in the survival rats

Compared with those on the 3rd day in group S, the concentrations of TP and ALB in group M decreased significantly while S/L and LDH increased significantly ($P < 0.05$) (Table 1); the concentrations of TP and ALB in group K decreased significantly while S/L, CK, and LDH increased significantly ($P < 0.05$) (Table 1); the concentrations of TP, ALB and GLB in group C decreased significantly while S/L and LDH increased significantly ($P < 0.05$) (Table 1); the concentrations of TP, ALB and GLB in group CP decreased significantly while AST, S/L and CK increased significantly ($P < 0.05$) (Table 1).

The concentration of AST in group CP was higher than that in group M, K, and C ($P < 0.05$) (Table 1); and the concentration of CRE in group CP was higher than that in group M ($P < 0.05$) (Table 1).

There were no significant differences in group M, C and group K ($P > 0.05$). (Table 1)

Changes of levels of TNF-α, IL-1β, IL-6 and IL-10 in intestine in the survival rats

Compared with group S in the 3rd day, the level of IL-10 in group M decreased significantly while IL-6 and TNF-α increased significantly ($P < 0.05$) (Table 2); the level of IL-10 in group C decreased significantly ($P < 0.05$) (Table 2).There were no significant differences in group K and CP compared with group S ($P > 0.05$). (Table 2)

Compared with group M, the levels of IL-6 and TNF-α in group K decreased significantly ($P < 0.05$). (Table 2)

There were no significant differences between group K and group C ($P > 0.05$). (Table 2).

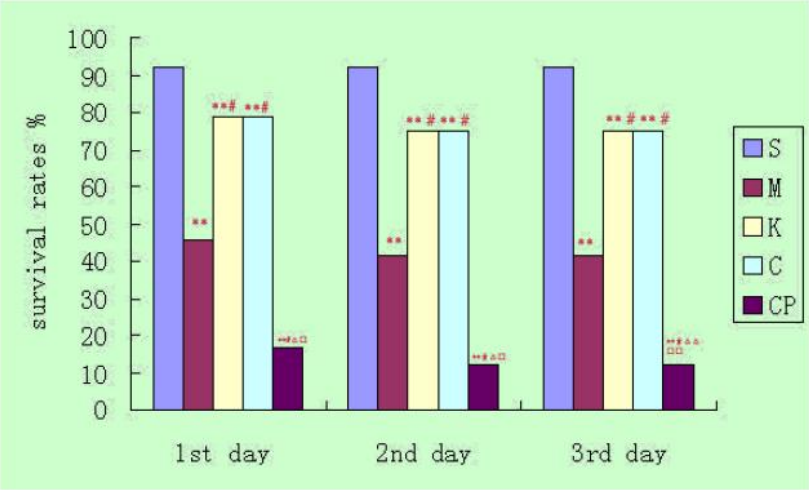

Fig. 2. Changes in the survival rate following 75 min intestine ischemia
Compared with group S: *$P < 0.05$, **$P < 0.01$; compared with group M: $^{\#}P < 0.05$, $^{\#\#}P < 0.01$; com-pared with group K: $^{\Delta}P < 0.05$, $^{\Delta\Delta}P < 0.01$; compared withgroup C: h$P < 0.05$, hh$P < 0.01$.

Table 1. Changes of serum biochemical indicator (mean ± SD)

	n	AST (U/L)	ALT (U/L)	S/L	TP (g/L)	ALB (g/L)	GLB (g/L)	A/G	BUN (mmol/L)	CRE (μmmol/L)	LDH (U/L)	CK (U/L)
S	8	82 ± 21	56 ± 30	1.6 ± 0.4	71 ± 4	32 ± 3	38 ± 3	0.9 ± 0.1	6.0 ± 1.1	33 ± 3	69 ± 23	126 ± 29
M	8	121 ± 27	37 ± 7	3.4 ± 1.4**	60 ± 9*	24 ± 2**	36 ± 8	0.7 ± 0.1	6.0 ± 0.9	25 ± 3	235 ± 92*	205 ± 104
K	8	118 ± 47	40 ± 12	2.9 ± 0.6*	59 ± 3*	24 ± 2**	35 ± 3	0.7 ± 0.1	5.1 ± 1.0	28 ± 4	160 ± 60*	338 ± 114**
C	8	114 ± 39	40 ± 12	2.9 ± 0.5*	55 ± 6**	24 ± 1**	31 ± 5*	0.8 ± 0.1	4.3 ± 0.9**##	28 ± 3	138 ± 34**	251 ± 147
CP	3	301 ± 91**##ΔΔhh	45 ± 19	4.6 ± 0.9**Δ	50 ± 12**	22 ± 5**	28 ± 8*	0.8 ± 0.1	5.3 ± 0.7	34 ± 6#	343 ± 61	41 ± 149**

Compared with group S:*P < 0.05, **P < 0.01; compared with group M: $^{\#}P$ < 0.05, $^{\#\#}P$ < 0.01; compared with group K: ^{A}P < 0.05, ^{AA}P < 0.01; compared with group C: hP < 0.05, hh$P$ < 0.01.

Changes of intestinal mucosa under light microscope and Chiu's score in the survival rats

The villus and glands were normal. No inflammatory cell infiltration was observed in mucosal epithelial layer insham group. Slight edema of mucosa villus and infiltration of few necrotic epithelial inflammatory cells neutrophil leukomonocyte were found in mucosa epithelial layer in M, K, C and CP groups. (Fig 3)

There were no significant differences in Chiu's score among the five groups on the 3rd day (P > 0.05). (Table 2)

Changes of counts of IMMC and ultrastructure in the survival rats

There were no significant difference in the number of IMMC among the five groups in the survival rats (P > 0.05) (Fig. 4, Table 2). The ultrastructure of IMMC was normal in the sham group. There were abundant vacuoles with reduced number of granules in their endochylema in groups M and CP. There were fewer swollen granules in IMMC homogeneity in groups C and K (Fig. 5).

Table 2. Changes of the levels of TNF-α, IL-1β, IL-6, IL-10, IMMC counts and Chiu's score in the intestine (mean ± SD)

	n	IL-10 (pg/mg)	IL-1β (pg/mg)	IL-6 (pg/mg)	TNF-α (pg/mg)	IMMC counts (n/field)	Chiu's score
S	8	33 ± 4	613 ± 194	6 ± 2	30 ± 11	24 ± 14	0.4 ± 0.5
M	8	21 ± 5**	657 ± 129	40 ± 16**	43 ± 5*	26 ± 11	1.0 ± 0.5
K	8	27 ± 3	750 ± 150	13 ± 5#	27 ± 7##	28 ± 13	0.6 ± 0.6
C	8	22 ± 5**	678 ± 170	29 ± 12**h	25 ± 8##	31 ± 12	1.0 ± 0.5
CP	3	34 ± 3	814 ± 234	28 ± 5	33 ± 5	29 ± 7	1.0 ± 1.0

Compared with group S:*P < 0.05, **P < 0.01; compared with group M: $^{\#}P$ < 0.05, $^{\#\#}P$ < 0.01; compared with group K: ^{A}P < 0.05, AAP < 0.01; compared with group C: hP < 0.05, hh$P$ < 0.01.

Changes of lung histology in the survival rats

The lung histological structure was normal in group S, while the lung tissues were obviously damaged with edema, hemorrhage, and inflammatory cell infiltration in groups M and CP, and the injury was ameliorated in groups C and K. (Fig 6)

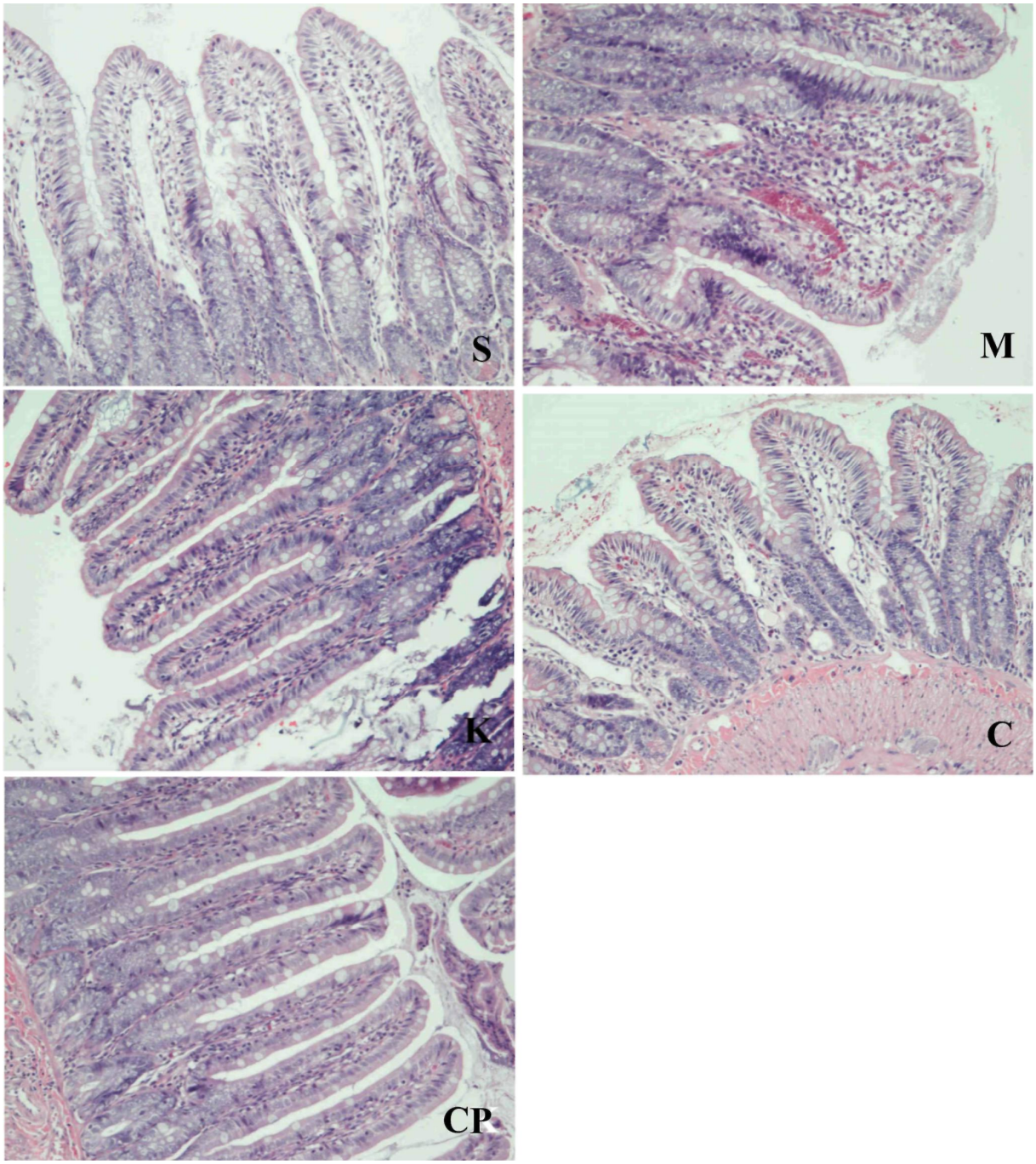

Fig. 3. Microscopic appearance after hematoxylin and eosin staining (x 200)
The villus and glands were normal and no inflammatory cell infiltration was observed in mucosal epithelial layer in sham group. Light edema of mucosa villus and infiltration of few necrotic epithelial inflammatory cells neutrophil leukomonocyte were found in mucosa epithelial layer in M, K, C and CP groups.

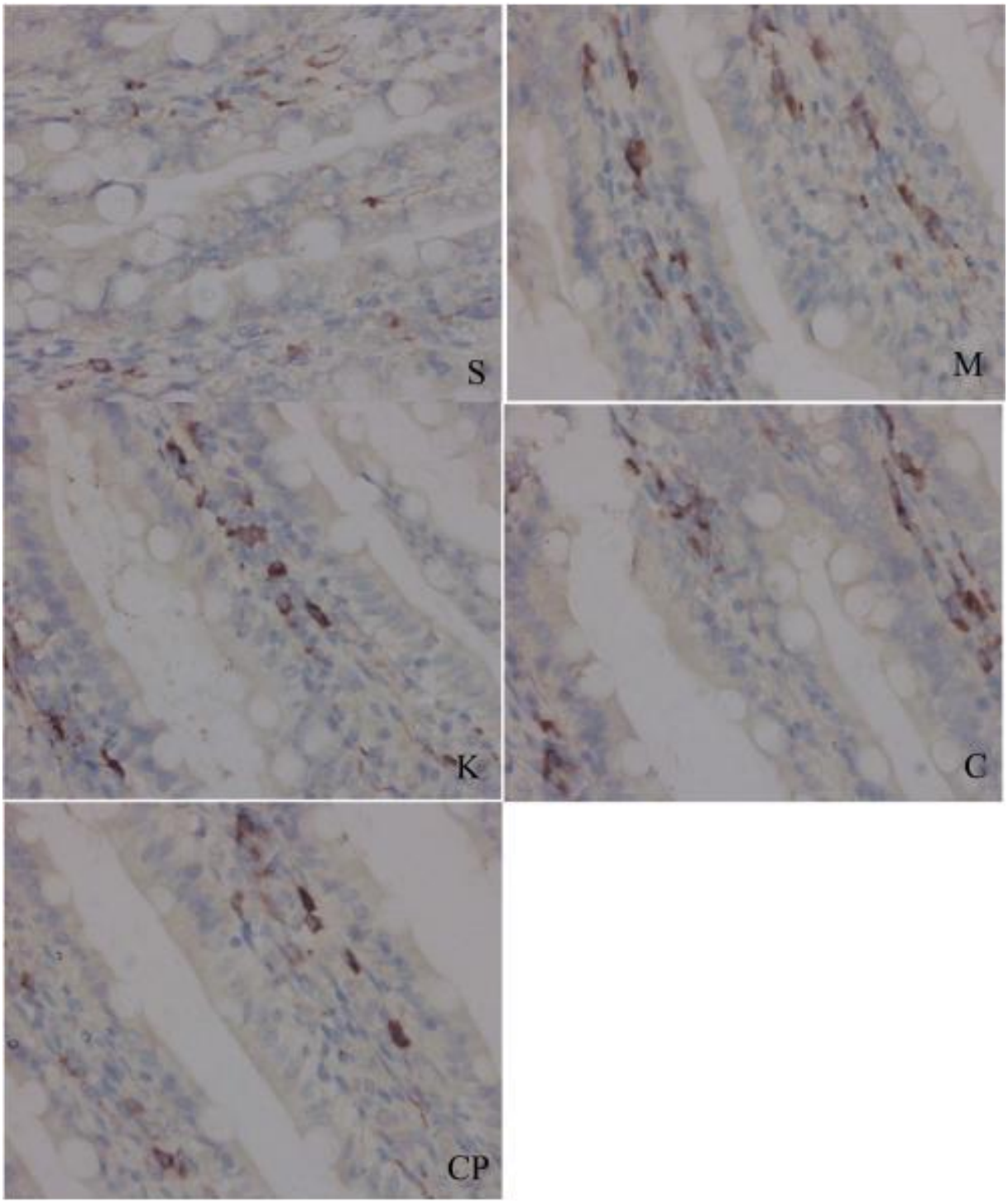

Fig. 4. Immunohistochemical detection of tryptase in small intestine of rats in each group (x 400)
Brownish granules in the cytoplasm were recognized as positive staining for tryptase.

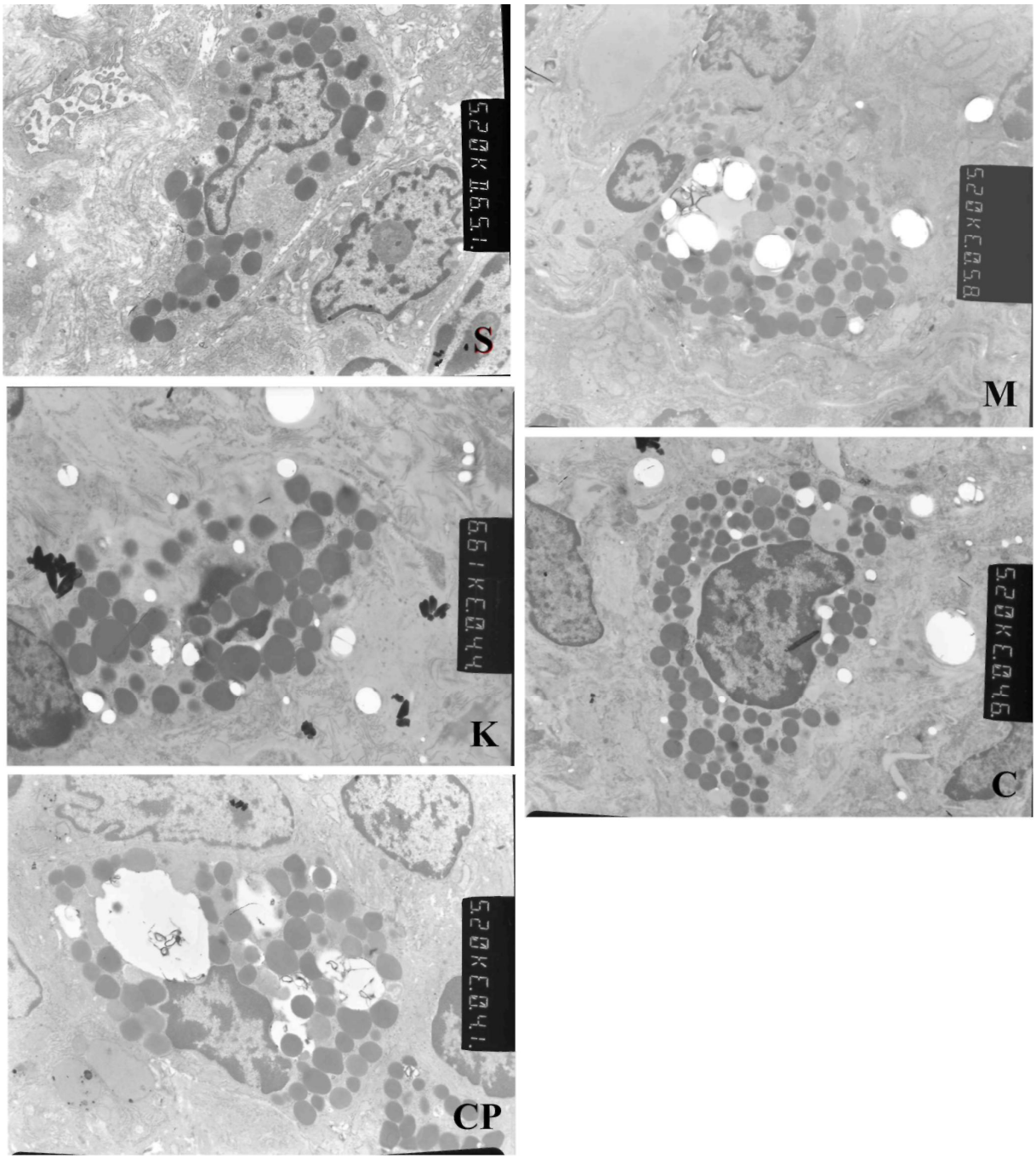

Fig. 5. Ultrastructure of intestinal mucosal mast cells of rats in each group (x 10, 000)
There are abundant vacuolus with a reduction in granulation in their endochylema in group M and CP; Granulation in endochylema is obvious (Is this right?). There is no vacuolus in their endochylema in the sham group. These changes in ultrastructure are ameliorated by treatment with Cromolyn Sodium and ketotifen in group C and K.

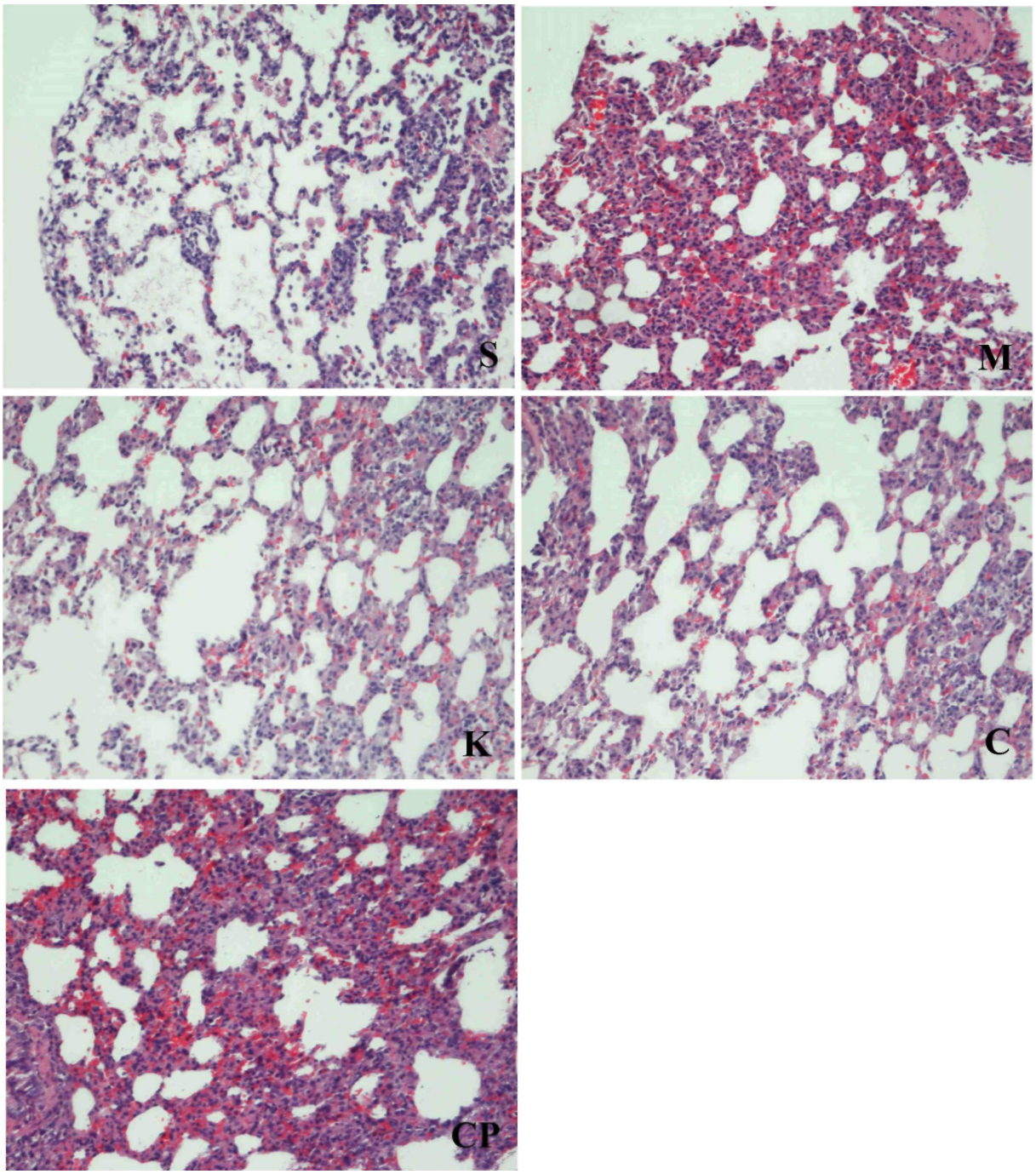

Fig. 6. Histological structure of lung of rats in each group (HE Staining, x 200)
The lung histological structure was normal in sham-operated group, while the lung tissues were obviously damaged with edema, hemorrhage, and inflammatory cell infiltration in group M and CP, and the injury was ameliorated in group C and K.

Discussion

IIRI is a significant problem in small bowel transplantation, abdominal aortic aneurysm surgery, cardiopulmonary bypass, strangulated hernias, and neonatal necrotizing enterocolitis [10]. Most reports about IIRI selected rats as the animal models. Differences in intestinal ischemia time would result in different survival rates after ischemia reperfusion. The ideal survival rate in intesti-

nal ischemia-reperfusion injury animal model should be 40%~50% after seven days as those survival could provide an ideal model for treatment or study. Our study found that with the prolonged intestinal ischemia time, the survival rate after ischemia reperfusion decreased significantly. The survival rates after intestinal ischemia for 75min were about 40%~50% during the 1st to 7th day after reperfusion in Sprague-Dawley rats. In addition, we observed most animals died on the 1st day after reperfusion, and there were almost no animals died on the 4thto 7th day after reperfusion. As a result, the ischemia time of 75 min and 3 days' reperfusion is appropriate in our study.

IMMC is an enriched source of inflammatory mediators such as histamine, prostaglandin D2, leukotriene, IL-3, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, IL-16, TNF-α, and more [11]. Boros and his lab reported that mucosal mast cell de-granulation plays an important role in the initiation of tissue injury after intestinal ischemia-reperfusion injury, and depletion of mast cells with compound 48/80 pretreatment prior to ischemia decreased the severity of mucosal damage [6]. Kalia found the survival rate increased significantly after ketotifen pretreatment [8]. Andoh A reported that intestinal ischemia-reperfusion treatment induce a marked increase in mucosal permeability and IMMC degranulation, while the mucosal permeability and IMMC degranulation are significantly attenuated in mast cell deficient Ws/Ws rats [5]. Our previous study also proved that IIRI induces IMMC degranulated and the histamine concentration in intestine decreased [12], administrated cromolyn sodium could attenuate intestinal damage caused by IIRI [13]. The above studies suggest that stabilization of mast cells or degranulation of mast cells prior to ischemia may be a key mechanism to protect the gastrointestinal tract from injury. However, the studies about the effects of stabilization or de-granulation of mast cells after ischemia on IIRI and the survival rate have not previously been well investigated.

Cromolyn Sodium (CS) is a mast cell membrane stabilizer, it can inhibit the mast cell degranulation and releasing of histamine, TNF-α, and other inflammatory mediators [14]. Ketotifen is a second generation histamine H2 blocker which has been used in the management of allergic disorders. In addition to histamine receptor antagonism, ketotifen has been found to inhibit the release of mast cell and neutrophil-derived proinflammatory mediators. Compound 48/80 is a condensation product of p-metoxyphenethylmethylamine and formaldehyde, and is a potent inducer of mast cell de-granulation in rats [15]. The dosage of the above drugs were selected based on previous reports [8, 16, 17]. We found the survival rates during the 1st to the 3rd day with CS and ketotifen treatment were increased significantly compared with group M, while it decreased significantly with Compound 48/80 treatment compared with group M. The results indicate that stabilization of mast cells or antihistaminic after ischemia can also increase the survival rates while de-granulation of mast cells after ischemia can decrease the survival rates.

We observed functional changes in multi-organs in the survival rats, and analyzed the reasons that caused the rats to die as the dead animals couldn't be analyzed. Reperfusion with oxygenated blood after sustained ischemia is necessary to recover normal tissue and organ function. Intestinal mucosa is one of the best recovered organs in 24hours after IIRI [18]. We also found there were no significant differences in Chiu's score among the five groups on the 3rd day in the survival rats. The results also demonstrated that intestinal mucosa can be easily recovered from IIRI, which may the main reason that explains why the mortality didn't increase after the 3rd day.

Surprisingly, we found that IMMC counts were the same in the survival rats in the five groups. Although there were abundant vacuoles with reduced numbers of granules in their endochylema after treatment with compound 48/80, and there were fewer swollen granules in IMMC homogeneity af-

ter treatment with CS or ketotifen. The results prove that compound 48/80 induces IMMC degranulation while CS and ketotifen inhibited IMMC degranulation. The findings indicated that inhibited IMMC from degranulation may increase the survival rates after IIRI.

Previous studies have shown the important role of TNF-α, IL-1β and IL-6 for reperfusion-induced tissue injury and lethality [19]. IL-10 has anti-inflammatory properties and reduces tissue inflammatory injury following ischemia and reperfusion injury [20]. Our study found that the level of IL-6 in intestine in group model increases significantly compared with group sham on the third day, while the level of IL-10 in intestine decreased significantly on the 3rd day. Treatment with cromolyn sodium and ketotifen can decrease the levels of TNF-α and IL-6 in intestinal significantly compared with group model. The results indicates that CS and ketotifen can also decrease inflammation after IIRI, which may be another reason for the increased survival rates after treatment with CS and ketotifen.

ALT is synthesized in cytoplasm and AST is synthesized in mitochondria. The increased ratio of S/L represents the severity of liver cell injuries. The increased CK and LDH reflects damages in myocardial cells peculiarly. TP respond to nutritional conditions and liver anabolic state. Our study found that the increased ratios of S/L, LDH and CK, and the decreased levels of TP in groups M, C and group K compared to group S in the survival rats. And the concentrations of AST and CRE increased significantly in group CP compared with group M. The lung tissues were obviously damaged with edema, hemorrhage, and inflammatory cell infiltration in group M and CP, and the injuries were ameliorated after treatment with CS and ketotifen. The above results indicates that intestinal ischemia could not only induce intestinal reperfusion injury but also induced remote organ injury such as liver, heart and lung [21-23], and the remote organ injury maybe one of the important reasons that cause the animal to die.

Conclusion

Intestinal mucosal mast cells play an important role in the intestinal ischemia-reperfusion injury. Treatment with CSand ketotifen prior to reperfusion and following reperfusion could increase the survival rates on the 3rd day, while treatment with compound 48/80 could decrease the survival rates. Inhibition of mast cells from degranulation provides a new treatment strategy to protect multipleorgan injury induced by intestinal ischemia reperfusion. (The first 3 days) after ischemia-reperfusion injury is themost important time period for treatment. However, inflammatory injury to the intestines and damages toremote organs 3 days after reperfusion still exist.

Abbreviations

CS: Cromolyn Sdium; CP: Compound 48/80; AST:glutamic-oxaloacetic transaminase; ALT: glutamic pyruvictransaminase; S/L: the ratio of AST compare ALT; TP: totalprotein; ALB: albumin; GLB: globulin; A/G: the ratio ofALB compare GLB; CK: phosphocreatine kinase; LDH: lac-tate dehydrogenase; BUN: urea nitrogen; CRE: creatinine; IIRI: Intestinal ischemia-reperfusion injury; IMMC: Intes-tinal mucosal mast cells.

References:

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DISCUSSIONS ABOUT PREVENTIVE SERVICES: A QUALITATIVE STUDY

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Background: Elderly minority patients are less likely to receive influenza vaccination and colorectal cancer screening than are other patients. Communication between primary care providers (PCPs) and patients may affect service receipt.

Methods: Encounters between 7 PCPs and 18 elderly patients were observed and audiotaped at 2 community health centers. Three investigators coded transcribed audiotapes and field notes. We used qualitative analysis to identify specific potential barriers to completion of preventive services and to highlight examples of how physicians used patient-centered communication and other facilitation strategies to overcome those barriers.

Results: Sharing of power and responsibility, the use of empathy, and treating the patient like a person were all important communication strategies which seemed to help address barriers to vaccination and colonoscopy. Other potential facilitators of receipt of influenza vaccine included (1) cultural competence, (2) PCP introduction of the discussion, (3) persistence of the PCP (revisiting the topic throughout the visit), (4) rapport and trust between the patient and PCP, and (5) PCP vaccination of the patient. PCP persistence as well as rapport and trust also appeared to facilitate receipt of colorectal cancer screening.

Conclusion: Several communications strategies appeared to facilitate PCP communications with older patients to promote acceptance of flu vaccination and colorectal cancer screening. These strategies should be studied with larger samples to determine which are most predictive of compliance with prevention recommendations.

Background

Influenza and colorectal cancer are preventable diseases that result in substantial morbidity and mortality. Influenza and its complications contribute to an estimated 250, 000 to 500, 000 deaths worldwide each year [1]. Each year, 1 million new cases of colorectal cancer are diagnosed globally and more than 500, 000 people die from the disease [2]. Even in the United States, despite the existence of effective means to prevent influenza [3], only 65% of adults aged 65 and older report receiving influenza vaccination during the previous 12 months [4]. Similarly, despite the availability of effective screening modalities [5-7], a large proportion of Americans are not being screened for colorectal cancer [8, 9].

As a result, an important priority of research on these health promotion behaviors must be to identify specific barriers which prevent older adults from engaging in them. The Precede/Proceed Model, developed by Larry Green and Marshall Kreuter [10], provides a valuable theoretical framework for considering such barriers because it reminds us that we must think beyond individual-level factors such as lack of knowledge and consider environmental contributors as well. The Precede/Proceed model defines three types of factors which influence behavior: predisposing, enabling, and reinforcing [10]. Predisposing factors are characteristics that motivate a person to engage in behavior. These can include beliefs, attitudes, or knowledge or demographic background factors thought to impact the likelihood of engaging in the behavior. Enabling factors include characteristics of the environment that facilitate the behavior, as well as skills or resources, such as health insurance or ease of transportation, which make it possible to engage in the behavior. Reinforcing factors are defined as rewards or punishments which fol-

low the behavior or are anticipated as a consequence of the behavior [10]. Expectations about the support of friends and family for a behavior are often viewed as important reinforcing factors.

Partially because some of these barriers are likely to be more prevalent for members of some racial and ethnic groups than for others, disparities in receipt of both influenza vaccines and colorectal cancer screening tests have been found between nonwhites and whites in the United States [11-15]. Such disparities are only partially explained by differences in access to care [16], nor do they seem to be fully explained by patient beliefs [17-20] or provider attitudes [21]. Rather, Kilbourne and colleagues suggest that a key component may lie in the clinical encounter between patients and providers [22]. This article explores the potential of studying patient-provider encounters among older adults.

The Institute of Medicine has suggested that various features of the patient-physician relationship may contribute to disparities [23]. Specific elements of the interaction which may play a role in the existence of disparities are the provider's skills or lack thereof in cultural competence and in communication [22]. For example, if providers fail to tailor messages appropriately about health promotion or disease prevention, that can lead to lack of adherence to the prescribed behavior [22].

As for provider communication, researchers have found "patient-centered communication" important to achieving better patient recall of information, treatment adherence, satisfaction with care, and health outcomes [24]. Patient-centered communication is exemplified by encounters in which "the patient's point of view is actively sought by the physician" [25].

Researchers seem to agree on three key areas or components of patient-centered communication: (1) developing an understanding of the patient as a person, (2) conveying empathy, and (3) finding common ground regarding treatment and goals of care or, in this case, prevention [26]. Understanding the patient as a person means reaching beyond the physical symptoms to understand other important aspects of the person's lifestyle or context [27]. The idea of empathy, or the patient's perception of the doctor as caring and sensitive, is thought to be important to compliance with recommended behaviors [27].

The third construct, finding common ground, is described as sharing decision-making responsibility between the physician and patient or empowering the patient. Sharing power or responsibility allows patients to play a more active role in decisions related to their care. This idea is in line with Williams, Frankel, Campbell and Deci, who write that "relationship-centered care, " is related to Self Determination Theory because one of its central components is autonomy support or "interacting with patients by taking full account of their perspectives, affording choice, offering information, encouraging self-initiation, providing a rationale for recommended actions, and accepting the patients' decisions" [28].

While a number of prior studies have audiotaped and observed patient-primary care provider (PCP) encounters [29-34], we are unaware of prior studies that have directly observed and analyzed in qualitative terms how PCPs and patients discuss prevention of colorectal cancer or influenza. We chose to study two preventive services in tandem to compare and contrast barriers of each and to explore how patient-centered communication and other facilitators were used to overcome those barriers.

To understand how aspects of the patient-PCP communication affect receipt of these preventive services, we performed a qualitative study, observing and audiotaping medical visits at two community health centers. We also studied systems of care, such as whether staff routinely identified patients as needing a particular preventive service, or whether systems barriers such as a long wait time for a colonoscopy appointment prevented completion of services. Our primary objectives were (1) to describe the dialogue between PCPs and elderly patients about in-

fluenza vaccines and colorectal cancer screening and (2) to identify both potential barriers to and facilitators of completion of these preventive services (including all three types of factors specified by the Precede/Proceed model and specific strategies for patient-centered communication).

Methods

We conducted an in-depth observational study of two urban community health centers in greater Boston. We initially identified five health centers with a high minority population over the age of 65; reasons that three of the five health centers did not participate included transition to an electronic medical record, changes in health center leadership, and physical damage to the health center from a car accident. Our study design involved administration of questionnaires, observation of office systems, and observation and audiotaping of clinical encounters. Trained research assistants performed these tasks. Two medical anthropologists assisted in developing the observation form. Two research assistants were bilingual in Spanish and in English; we trained four additional interpreters to assist with Spanish and Haitian Creole-speaking patients. We also conducted in-depth interviews with key informants at each health center (medical directors, nurse managers, and nurses) to provide a context of systems and community factors.

Participants

In the fall of 2005, we recruited participants from two health centers. Research assistants approached a convenience sample of patients who presented to the health centers during the recruitment period (October to December 2005, the time of year when the influenza vaccine is available and most discussion about vaccination takes place). We informed patients that the purpose of the study was to "learn how doctors and nurses talk with older patients about their health, " and offered patients a $10 cash incentive to participate. The research assistants asked whether the patients had received any of the following preventive services: a vision test in the past year, a hearing test in the past year, a pneumonia vaccine ever, and an influenza vaccine since August 2005. We deliberately asked about multiple preventive services in an effort to blind the study's primary objective, which was to observe discussions about the influenza vaccine and about colorectal cancer screening.

Patients who were aged 65 or older, who spoke English, Spanish, or Haitian Creole, and who had not received an influenza vaccine in the current year were eligible to participate. After determining the patient's eligibility for the study, the research assistants asked patients whether they would be willing to have their appointment observed and audiotaped. Study investigators also approached PCPs (physicians and nurse practitioners) at each site, obtaining their permission to have encounters observed and audiotaped. We told the PCPs that they were participating in a study to examine communication between patients and providers about preventive services. We audiotaped and observed a total of 18 clinical encounters involving 7 PCPs. Eleven patients refused to participate in the study, and 20 patients were ineligible to participate because they had already received the influenza vaccine. The Institutional Review Boards at Cambridge Health Alliance and at RTI International approved the study; all patients and providers gave written informed consent.

Data collection

Prior to their visit, patients completed a brief survey that included questions about the purpose of the visit, health care use, risk factors for complications of influenza, and demographics. Following the visit, patients answered questions about their perceptions of the visit; their beliefs and attitudes about influenza vaccines, colorectal cancer screening, and mammography (women only); and additional demographic questions. PCPs completed a background questionnaire about their demographics. Research assistants set up a digital voice recorder in the exam room and remained in the exam room unless requested to leave by either the PCP or the patient. In only one encounter did the observer need to

leave the room. The research assistant observed and made notes about the PCP/patient interaction, and stood behind a curtain during the physical examination. The research assistants received training to observe aspects of the encounter including physical contact between patient and PCP, use of hand gestures, eye direction, facial expressions, listening, interruptions, and level of comfort. One investigator (KEL) reviewed both paper and electronic medical records 9 months after the visit to determine whether preventive services (immunization for influenza and colorectal cancer screening) were completed. In the one case where the record did not provide the necessary data, a research assistant spoke to the patient by telephone to obtain further information.

Analysis

We obtained verbatim transcriptions of all encounters, and identified all segments in which the providers and patients discussed either influenza immunization or colorectal cancer screening. For most of the Spanish-language encounters, a bilingual research assistant (JM) who observed the encounters both transcribed and translated the text of the encounter. We also analyzed detailed descriptive field notes that research assistants recorded during the observed encounters. An analysis team composed of a primary care physician-researcher (KEL), a nurse researcher (JEM), and a health behavior specialist (JH) read through all transcripts and field notes and discussed the details of each encounter. We identified potential barriers to and facilitators of completion of preventive services that emerged in these discussions, as well as specific patient-centered communication strategies. We reviewed and critiqued interim versions of the main barriers and facilitators in an iterative process. We present the barriers and facilitators upon which all three analysts and the study team agreed.

Results

Description of health centers and systems for promotion of preventive services

Health center 1, located in a city west of Boston, serves mainly African American and Haitian patients. This health center uses paper charts, does not use a flow sheet to track preventive services, and has no reminder system in place for preventive services. A nurse at this site educates patients about preventive services, particularly colorectal cancer screening (many patients, after seeing the gastroenterologist, have questions about how to complete the preparation for the test). However, most patients do not routinely see a nurse to discuss preventive services. During influenza season, staff post signs inside and outside the health center advertising influenza clinics. Patients are then able to walk in and obtain an influenza vaccine at the center without an appointment. We were only able to recruit two patients for the study at this site. Barriers to recruitment included a lack of availability of a Haitian Creole interpreter and a high number of patients who walk in for care without a previously scheduled appointment. We could not include patients who walked in because we were unable to anticipate research staff requirements (observer and interpreter) for these patients.

Health center 2, also located in a city west of Boston, serves a large Latino patient population. This health center uses an electronic medical record with an electronic flow sheet for tracking age-appropriate preventive services. The center staff called patients with diabetes (from a diabetes registry) to come in for an influenza vaccine. We recruited 16 patients for the study (both with and without diabetes) at this site; we suspect that our use of a bilingual Hispanic research assistant (JM) facilitated recruitment.

At each health center, both PCPs and nurses administered influenza vaccines to patients. Cost was not a barrier to receipt of the influenza vaccine at either health center. Structural factors impeded colorectal cancer screening efforts at both health centers: there was a long wait for routine colonoscopy appointments (approximately 9 months), and neither center had a system in place to track distribution and return of fecal occult blood testing (FOBT) cards.

Patient-PCP encounters

We observed 18 unique patient visits to 7 different PCPs. Table 1 shows the demographic characteristics of the 18 patients. Most were female, nonwhite, Spanish-speaking, poor, and with a low level of education. The mean age of participants was 71.9, and all had some form of health insurance. PCPs were physicians and nurse practitioners, trained in either family medicine or in internal medicine. Most of the PCPs were nonwhite, spoke Spanish fluently (although none identified as being Hispanic), and had practiced at their respective health center for at least 6 years. The average patient-PCP encounter length was 24 minutes.

PCPs and patients discussed the influenza vaccine in 16 of 18 (88.9%) encounters. The influenza vaccine was not discussed in the following two situations: (1) in a visit that took place prior to the availability of the influenza vaccine and (2) in an urgent care visit for a complaint of a red eye. In most cases (14 of 16 [87.5%]), the PCP introduced the subject of influenza vaccination. In 13 of 16 encounters the PCP vaccinated the patients; in the remaining encounters, a nurse vaccinated one patient after the PCP visit, a second patient refused the vaccine, and a third patient was ill and needed to return for the vaccination. The latter patient did not return to the health center to be vaccinated. When we called this patient several months later, she reported that she was preparing to have knee surgery and was unable to return for her influenza vaccine because she had difficulty walking.

PCPs and patients discussed colorectal cancer screening in 8 of 18 (42%) encounters. In four of eight encounters, the patients were either out of the age range for screening (age > 80) [35] or had already been screened. In the remaining four patients, three were screened during the follow-up period (two patients completed colonoscopy and one patient completed FOBT cards). One patient (the same patient who did not return for the influenza vaccine) did not complete FOBT cards because she had been ill. She also assumed her colon was normal because she had had many tests prior to her knee surgery, and felt that if she had a colon problem those tests would have detected it.

Table 1. Community Health Center Patient Characteristics (n = 18) Characteristics

Characteristics	
Female (%)	77.8
Mean Age (se)	71.9 (7.8)
Race (%)	
White	22.2
Black	16.7
Mixed	27.8
Other	33.3
Hispanic or Latino origin (%)	72.2
Insurance (%)	
Medicare	77.8
Medicaid	16.7
Free Care	5.5
Language used in visit (%)	
English	27.8
Spanish	72.2
Education (%)	
< High School	66.7
High School diploma	11.1
Some higher education	22.2
Annual Income (%)	
< $10,000	44.4
$10,000–$14,999	5.6
$15,000–$19,999	16.7
$20,000–$25,000	11.1
Don't know/missing/refused	22.2

Use of patient-centered communication and other facilitation strategies to overcome barriers

Through direct observation of visits and analysis of transcripts of the audiotaped encounters, we identified examples of all three types of barriers described in the Precede/ Proceed framework (predisposing, enabling, and reinforcing). Table 2 lists these potential barriers.

We then identified ways in which patient-centered communication and other strategies (including cultural competence) were used to address barriers to acceptance of influenza vaccines and colorectal cancer screening. Table 3 provides specific examples from the patient encounters of patient-centered communication strategies and other facilitators.

Sharing of power and responsibility was the most frequently used patient-

centered communication strategy (see Table 3). In the first example, the provider brings up the topic of colonoscopy and asks the patient to think about it: PCP: "I also would like to talk to you about the colonoscopy. Have you had it done in the past?" PCP explains colonoscopy. "You can think about it, if you would like to have it done, this test, but it is possible." The provider returns to the topic after vaccinating the patient. "Okay, what do you think of the possibility of having done the colonoscopy test?" In this case, the provider is not telling the patient what to do, or even strongly recommending it, but merely presenting the information and asking the patient to consider it. The power to make the decision is left to the patient. When the patient decides it would be a good idea, the provider assists in scheduling the test at a time that would be convenient for the patient.

Table 2. Barriers identified from patient-provider encounters

Precede/Proceed construct	Barrier
Predisposing factors (beliefs, attitudes, knowledge, demographics, background)	Fear of becoming ill from influenza vaccine No symptoms of colorectal cancer
Reinforcing factors (rewards or punishments which follow the behavior or are anticipated as a consequence)	Anecdotes of negative experiences with influenza vaccine
Enabling factors (environmental factors, such as health insurance, cost, and structural barriers, such as ease of access to care)	Patient unable to receive influenza vaccine during visit due to acute illness Dependence on others for transportation makes return visits more difficult to schedule Misunderstanding/misinformation about cost of influenza vaccine Complexity of colorectal screening process Many topics covered in visits

Example 2 demonstrates how a PCP is able to convince a patient, initially reluctant to have an influenza vaccine, to receive the vaccine by the end of the visit. The PCP uses several tools to facilitate the patient's acceptance of the vaccine: he or she revisits the topic throughout the encounter, giving the patient an opportunity to think about it, and empowers the patient by allowing her to choose which arm for the injection.

In another example (Example 6) the physician uses these same strategies of shared power and revisiting the topic multiple times to try to convince a patient to have the colonoscopy. In this example, the physician asks the patient, "There is one test you haven't done, this is a test called 'colonoscopy, ' have you heard of this test?" The patient responds, "You told me last time, you asked me to think about it, but..." PCP: "What did you think? You didn't like the idea." P: "I don't like the idea. I imagine it is because I am feeling fine, maybe because I think illness gives you signs."

The physician clears up the misinformation by explaining that often when signs appear it is too late for early detection and cure, and that this is why the screening is important. But sensing that the patient is unconvinced, the physician goes on to explain that another alternative is FOBT cards. The physician is successful in convincing the patient at least to agree to take home FOBT cards. However, the patient does not return the cards to the office (see Table 3).

Empathy

An example of empathy occurred when one patient expressed how painful the vaccinations (one for flu and one for pneumonia) were (example 8). She said to the doctor, "These shots hurt a lot: I think they make them for horses...I don't think you ever had one doctor, you should have one." The PCP responded that indeed she had received the vaccinations, which let the patient know that she could relate to her pain.

Table 3. Examples of patient-centered communication strategies and other facilitators used by PCPs to address barriers

Barrier	Example from transcript	Patient-centered communication strategy	Other facilitators	Outcome
Lack of knowledge about CRC	**Example 1: 66-year-old, Spanish-speaking Hispanic male** PCP: I also would like to talk to you about the colonoscopy. Have you had it done in the past? Would you remember what it is about? PCP then explains colonoscopy. PCP: You can think about it, if you would like to have it done, this test, but it is possible. PCP returns to CRC discussion after giving shots. PCP: Okay, what do you think of the possibility of having done the colonoscopy test? P: It would be good, right? PCP tries to schedule GI appointment at best time for patient.	Shared power/common ground		GI appointment scheduled
Anecdotes of negative experiences with influenza vaccine	**Example 2: 66-year-old Spanish-speaking Hispanic woman from Puerto Rico** PCP: I don't know if you want to get the shot against the flu? P: Ay no! PCP: Why not? P: I have never gotten it before because I heard it gives people...My brother in law got it and he was in the hospital for more than a month with the flu, with fever, vomits, he got everything. 'Ay, cunada don't do it' (sister-in-law, don't get the flu shot!) so I never got it. No, no, I won't do it. PCP tries to convince patient that reaction is a very rare event, recommends strongly, gives patient a chance to think about it during the visit. Later in visit: PCP: And what have you thought about the shots? P: (laughed) Ay doctor, I am not frightened by the injection, I am afraid of the reaction, such as fever or something like it. PCP: Would you like to try it, the reactions are rare, but you are the one who has to make the decision. PCP negotiates which arm to apply shots, given that she has arthritis in one arm – decides shots should go in bad arm so will still have one good arm. PCP: Very well, congratulations!	Shared power/common ground	PCP initiates discussion of influenza vaccine Revisiting the topic throughout the encounter	Patient receives vaccine during exam
Mis-understanding/ misinformation about cost of influenza vaccine	**Example 3: 66-year-old Spanish-speaking Hispanic man (Salvadoran)** PCP explores patient's reason for not getting flu shot: Patient doesn't think he will get the flu. Also, doesn't want shot because is worried will get billed for it (last year he received a bill for it, and for PCP visit, has Medicare only). PCP decides to change way will bill for visit; not as PE but for cholesterol and stomach problems. PCP: Ah...what else...if I can give you the shot without any charge, would you have done it today? P: Yes. Later in visit PCP assesses patient's literacy in English, gives Medicare website to patient (patient's son reads English and has Internet).		Cultural competence (assesses English literacy before giving patient written information) PCP addresses incorrect beliefs/mis-information	Influenza vaccine is given during exam

Table 3. Examples of patient-centered communication strategies and other facilitators used by PCPs to address barriers (Continued)

Dependence on others for transportation makes return visits more difficult to schedule	**Example 4: 66-year-old Spanish-speaking Hispanic woman (from Dominican Republic)** PCP tries to make appointment at a convenient time for patient. PCP: When do you prefer the appointment? P: In the afternoon. In the morning she is working (referring to her daughter sitting next to her). PCP: What time is good for you? (Asking patient's daughter.)		Adapting to each patient's needs Facilitates scheduling of colonoscopy	Colonoscopy was scheduled
Patient does not speak English	**Example 5: 69-year-old Spanish-speaking male from El Salvador** PCP is talking in Spanish to patient, but PCP doesn't speak fluent Spanish.		Cultural competence	Influenza vaccine given during appointment; CRC screening not discussed, but patient has GI appointment in 2 days for weight loss
No symptoms of colorectal cancer	**Example 6: 66-year-old Spanish-speaking Hispanic woman** PCP: There is one test you haven't done, this is a test called "colonoscopy," have you heard of this test? P: You told me last time, you asked me to think about it, but.. PCP: What did you think? You didn't like the idea. P: I don't like the idea. I imagine it is because I am feeling fine, maybe because I think illness gives you signs. PCP: The problem is that illness gives you signs when it is too late, and we have found that the way of finding out about it when there is still a cure for it, and this is the main purpose of this test. If you don't want to have this test done, there is another way of doing it, an easy way, I don't know if you have seen our cards, we will do this test every year. This is another way, it is not as good as the colonoscopy, but it is a way to do an evaluation, if you wish we can do it [FOBT]. In the lab you will get the cards and take them home with an envelope to send them back.	Shared power/common ground	Revisiting the topic between encounters	Patient does not return FOBT cards. When called several months later, she reported that she did not complete the cards because she has been ill. She also assumed her colon was normal because she had had many tests prior to her recent knee surgery and felt that if she had a colon problem those tests would have detected it.
No specific barriers (communication strategies used in normal course of visit)	**Example 7: 87-year-old Spanish-speaking Hispanic woman (from Colombia)** (Patient has lung, heart conditions.) Observer asked to leave room, tape turned off at one point. Patient hugged PCP, was crying. PCP not rushed at all, took her time. PCP very friendly toward patient, paid attention, listened carefully.	Empathy		Patient did get flu vaccine during exam; not in age range for colonoscopy
	Example 8: 66-year-old Spanish-speaking Hispanic woman from Dominican Republic (same patient as example 4) PCP: ...after you had the surgery, this is nothing. (Trying to give comfort to patient while applying the shots.) P: These shots hurt a lot: I think they make them for horses...I don't think you ever had one doctor, you should have one. (Laughed) PCP: Yes, yes, I did it already. (Laughed.) Somebody else gave it for me. (Laughed)	Empathy		

Patient as person

Although it did not appear to be relevant to a specific preventive service barrier, one example (not in the table) of the "patient as person" construct occurred when a provider acknowledged a patient's upcoming vacation before introducing the topic of vaccination, saying, "Well, you just want to go Miami! Okay, one thing that you need is to have the flu shot given..." The results of treating a patient as a person were often observed in the high five with which a provider greeted an 83-year-old AfricanAmerican patient, and the way in which this relationship helped a patient to overcome fear of immunization.

Cultural competence

There were several obvious examples in which cultural competence played a role. In one case, even though a provider was not fluent in Spanish, she spoke Spanish to her patient during the visit (Example 5). In another, the physician assessed the patient's English literacy before providing an English version of some Medicare information regarding the cost of the vaccine (Example 3).

Other facilitators

There were also several instances of a strong bond or relationship between patients and providers. In some examples, they hugged, gave each other high five or even expressed feelings of love for each other. In one example, the patient brought the provider a gift.

In another example (a 66-year-old Spanish-speaking patient), while the physician was out of the room, the patient was speaking to her daughter about possibly changing health centers on the advice of her sisters. The patient related that her sisters say to her, "It's like you got married with that doctor." Describing her 20-year relationship with the PCP, the patient said that her PCP loved her and has helped her a lot, and is like a family member to her. At the end of the visit, the patient says to her PCP, "I love you very much, " and the two hug.

Our observation of a trusting relationship between PCP and patient was corroborated by the fact that in the postvisit debriefing questionnaire, all of the patients who completed the questionnaire (17 of 18) strongly agreed with the statement "All in all, I have complete trust in [PCP name]."

Discussion

In this qualitative study, we observed that the following factors appeared to facilitate receipt of an influenza vaccine: patient-centered communication strategies, including shared power and responsibility, empathy and treating the patient as a person, cultural competence, PCP introduction of the influenza vaccine discussion, PCP vaccination of the patient, persistence of the PCP (revisiting the topic throughout the visit), and strong rapport and trust between the patient and PCP. We noted significant barriers to receipt of influenza vaccines: (1) acute viral illness (where the illness was perceived to be a contraindication to vaccination), and the patient had to postpone his or her influenza vaccine, requiring another trip to the health center; and (2) an urgent care visit for an acute complaint (as opposed to a routine health care maintenance visit) where preventive services were not discussed. Similar to the case of influenza vaccines, we found that patient-centered communication, the PCP's persistence, and strong rapport and trust between patient and PCP seemed to facilitate completion of colorectal cancer screening. Additional potential facilitators of colorectal cancer screening included the presence of someone else at the visit with the patient, and the PCP's assistance with scheduling. Barriers to colorectal cancer screening included (1) lack of symptoms suggesting a problem with the colon and (2) acute illness that made it difficult for a patient to return the FOBT cards to the health center.

Our observation that most PCPs discussed influenza vaccination with their patients appears to contradict prior studies that have shown much higher "missed opportunities to vaccinate" [36]. We suspect that our

finding may reflect observation bias: because the PCPs knew we were observing discussions of preventive services, they may have been more likely to discuss vaccination. Our observation that trust between PCP and patient seemed to be associated with high use of recommended preventive services is consistent with prior studies [37]. Why did we observe such a high level of trust between the PCPs and their patients? It is possible that patients who agree to be observed may be more trusting than other patients. It is also possible that the population we studied, mostly Hispanic patients from El Salvador, Guatemala, Colombia, the Dominican Republic, and Puerto Rico, are particularly trusting of their PCPs. Among diverse populations of Hispanic patients, Mouton and Villa [38] have described a cultural phenomenon known as *personalismo*. *Personalismo* is an "inclination to relate [to] and trust individuals as opposed to systems or organizations." Such a level of trust was exemplified by the touching and hugging we observed, as well as by the verbal expression of mutual love and appreciation between patients and their PCPs. Finally, we observed a high level of race and language concordance between patients and PCPs. It is possible that such concordance, coupled with the fact that most of the PCPs had worked at their respective health centers for many years, contributed to the high level of trust we observed.

We observed a number of instances in which providers attempted to share the responsibility or power of decision making by providing the patient with the information about the preventive measure and then giving him or her time to decide whether to have the vaccine or schedule the colonoscopy. Phrases such as, "it's your decision" or "what have you decided?" were common. Stewart et al. found that interactions which scored high on patient-centeredness were actually associated with better emotional health 2 months later [25]. Other research has found that patients are more satisfied when interactions are patientcentered [39]. Thus, they may be more likely to adhere to recommendations that are patient-centered.

PCPs went "above and beyond" their usual responsibilities when they vaccinated patients during the encounter, and when they helped patients to schedule appointments. Given that PCPs report lack of time and a large number of preventive health issues they must address [40], having non-physician members of the health care team perform these tasks might enable PCPs to address other issues. Yet PCP discussion of preventive health services conveys a credibility and importance that can be particularly motivating to patients [41, 42]. Moreover, several studies report that even busy physicians are able to talk to their patients about receiving adult immunizations [43]. We also observed that PCPs tailored their approach to discussing preventive services to the unique circumstances of each patient, demonstrating the practice of the "art" of medicine.

Our study is limited by the fact that we observed only a small number of patient-PCP encounters in two urban health centers. Among these encounters, we observed only four discussions of colorectal cancer screening in patients who were eligible for such screening. In addition, we do not have demographic data on patients who refused or were ineligible to participate. Thus, it is unclear whether this sample of patients is representative of patients engaged in primary care in Boston-area community health centers. Similarly, we do not know whether the practices of the observed PCPs (such as helping patients to schedule appointments or vaccinating patients) are representative of all PCPs who practice in community health centers. Our study required that an observer be present while patients were treated. This could have had a large impact on the conversation between doctor and patient. Another limitation was that we provided a cash incentive to participate. This may have influenced the validity of the information provided on the patient surveys. Due to study logistics, we were not able to include patients who walked in at health center 1. Thus the two patients we re-

cruited at that site may not be representative of patients at that health center.

Conclusion

Though not without limitations, our study is unprecedented. It provides valuable observations about how PCPs use patient-centered communication strategies to complete preventive services in disadvantaged elderly patients seen at community health centers. We observed that most influenza vaccines were given during the exam by the PCP and that the majority of the PCPs knew their patients for long periods and/or had established trusting relationships with them. During the observed exams, many PCPs were able to take the time to revisit preventive issues several times. In addition, in some cases, PCPs were also able to empower patients, to empathize with them, to correct misinformation, and to provide assistance in arranging follow-up. All these factors appear to influence the completion of influenza vaccination, and some of them may also impact the completion of colorectal cancer screening. Such observations warrant further study in a larger sample of patients, and may help to inform the design of interventions to increase rates of influenza vaccination and colorectal cancer screening in patients seen at community health centers. This study identified a number of potential barriers to these two screening behaviors and examples of how providers used patient-centered and culturally competent communication to address them. A larger study might include these measures to determine which are most predictive of compliance. Such research would help to illuminate which factors physicians should focus on in a time-limited appointment and which strategies are most effective in helping to promote these prevention strategies in minorities and, thus, help to reduce disparities.

Authors' contributions

KL, co-principal investigator, led clinic recruitment, led analysis, and wrote and edited drafts of the manuscript. BK participated in analysis and drafting of the manuscript. JEM, study coordinator, oversaw training, patient recruitment, and data collection. JM coordinated data collection in one clinic and translated Spanish-language interviews into English. SH, KI, DO, and NP participated in data collection and analysis of results. BW participated in the initial study design and interpretation of findings. JH, the principal investigator, led study design and participated in the analysis and writing of this manuscript. All authors read and approved the final manuscript.

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CHANGES IN THE PATTERN OF SERVICE UTILISATION AND HEALTH PROBLEMS OF WOMEN, MEN AND VARIOUS AGE GROUPS FOLLOWING A DESTRUCTIVE DISASTER: A MATCHED COHORT STUDY WITH A PRE-DISASTER ASSESSMENT

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Objectives: Female gender and young age are known risk factors for psychological morbidity after a disaster, but this conclusion is based on studies without a pre-disaster assessment. The aim of this study in family practice was to investigate if these supposed risk factors would still occur in a study design with a pre-disaster measurement.

Methods: A matched cohort study with pre-disaster (one year) and post-disaster (five years) data. Community controls (N = 3164) were matched with affected residents (N = 3164) on gender, age and socioeconomic status. Main outcome measures were utilization rates measured by family practice attendances and psychological, musculoskeletal and digestive health problems as registered by the family practitioner using the International Classification of Primary Care (ICPC).

Results: Affected residents of female and male gender and in five age groups all showed increases in utilization rates in the first post-disaster year and in psychological problems when compared to their pre-disaster baseline levels. The increases showed no statistically significant changes, however, between women and men and between all age groups.

Conclusion: Gender and age did not appear to be disaster-related risk factors in this study in family practice with a pre-disaster base line assessment, a comparison group and using existing registries. Family practitioners should not focus specifically on these risk groups.

Background

Disasters often have an effect on the victims' health and health problems than men in the aftermath of a disaster victims present more psychological and physical health problems as a result. Within this context, several risk groups may be distinguished, as gender and age, which have been described after many disasters [1].

Most of the studies found that women present with more related to earthquakes and hurricanes [2-7]. Some studies showed other results, however, in which men appeared to be more vulnerable than women [8, 9]. In her review using 160 studies about the health problems after disasters, Norris [1] concludes that in 49 studies a statistically significant gender difference was observed in post disaster stress, distress or disorder. Of these, 46 studies found female survivors to be more adversely affected, especially for developing a Posttraumatic Stress Disorder (PTSD). In a meta-analysis Brewin found that when men and women were directly compared within the same study, women were more at risk of developing PTSD holding constant the type of trauma [10]. Finally, Tolin & Foa conducted a meta – analysis on sex differences in trauma and PTSD, using 290 studies published between 1980 and 2005. Their general conclusion was that females were more likely than males to meet criteria for PTSD, although females were less likely to experience potentially traumatic events [11].

Some studies on the effect of age in presenting post-disaster health problems showed that middle aged (40–65) victims were most distressed [6, 9, 12] and showed a higher utilization of health care services [13]. Two groups of different ages were compared in most of these studies and the results showed that the older group (65+ years) presented with fewer symptoms of distress or depression. The inoculation theory has to be mentioned in this context, viz. that victims with more experience of life and its major

and minor (personal) disasters are more resilient to the effects of a "new" disaster than "inexperienced" victims [12, 14-16]. Contradictory results are found too, however, and several studies have shown elderly Japanese, Polish and Australian victims of natural disasters to be more at risk of post-disaster distress than younger groups [17-19]. In general, however, older victim groups are more resilient to the effects of a disaster than younger groups [1].

Almost all studies referred to above are based on designs that did not use pre-disaster data and used a cross-sectional, retrospective design with short-term follow-up, using (self-report) questionnaires. In the reviews and meta – analysis mentioned above [1, 10, 11] it was suggested that the design of the study strongly influenced outcomes and results. Retrospective studies were associated with weaker effects for female gender and stronger effects for younger age and the effect size was greater when respondents were interviewed rather than given questionnaires. Epidemiological studies were associated with a significantly greater sex difference in PTSD than were convenience-sample studies.

Moreover, most studies discussed gender and age differences concerning PTSD, while in family practice (or primary care in general) this disorder is not often diagnosed. After disasters family practitioners often diagnose other psychological problems (anxiety, depression, disturbances of sleep, concentration or memory) and/or physical symptoms. In addition, we know of no studies in family practice of gender and age as possible risk factors for post-disaster health problems.

On 13 May 2000 a fireworks depot exploded in a residential area of Enschede, a city with 125, 000 inhabitants in the eastern part of the Netherlands. As a result, 18 residents and 4 firemen were killed and about 1, 000 people were injured. Some 1, 200 victims lost their homes and personal belongings and had to be relocated for some years. Baseline data were available after the disaster, because the health problems of (future) victims and controls had already been registered by the family practitioner in the period prior to the disaster. This enabled us to investigate health problems longitudinally, therefore, with the inclusion of pre-disaster utilization rate and morbidity.

The aim of this study was to explore whether the supposed risk factors of female gender and younger age would (also) appear in a study in family practice in which a pre-disaster baseline measurement was available with a longitudinal design, without recall bias and using a comparison group.

We hypothesized that women and members of the younger age groups will have, for several years post disaster, elevated rates of psychological problems and physical symptoms and an increased utilization compared to their pre disaster baseline, to members of a comparison group and compared to men and older age groups.

Methods

Setting

Every citizen of the Netherlands is registered with one family practitioner (FP), who acts as a gatekeeper to secondary care. This means that patients affected by the disaster and their medical histories were already known to their FPs in the period prior to the disaster. All participating FPs were already using electronic medical records (EMR). Thus in this study, it was possible to collect data from one year prior to the disaster and the study period continued until 5 years after the disaster.

All 60 FPs in Enschede were asked to participate in this study and 44 of them agreed. The sixteen FPs who refused to participate gave three different reasons; six expected an increase in workload, nine had no victims in their practices, and one did not use an electronic data system.

Patients were informed about their FP's participation in this study by posters and leaflets in the waiting room and by announcements in the local newspapers. They were entitled to object to the use of their anonymized data, but nobody did. The study was carried out according to Dutch legislation on privacy. The privacy regulation of the study was

approved by the Dutch Data Protection Authority [20]. According to Dutch legislation, neither obtaining informed consent, nor approval by a medical ethics committee was obligatory for this observational study.

Matching variables

After the disaster (as after many others) it was problematic to identify exactly who had been directly affected by the disaster, not at least because of the various possible definitions of 'affected', including the concept 'exposed'.

To overcome this problem two external sources were used: persons were either marked as affected in the patient registration of their FP (using the zip-codes of the affected area or because being affected was mentioned in the patient – practitioner encounter), or were registered in the database of the municipal Information and Advice Centre (IAC); residents were for example registered here to acquire a new house and for financial compensation. The two databases were compared and inconsistencies were corrected. Despite our efforts, we are not completely sure that every single person in our study was directly exposed to the explosions, while we are pretty sure they were all affected. By way of precaution, we will not use 'victim', but 'affected resident'.

All victims had to be registered with one family practice during the entire study period, from 13 May 1999 until 13 May 2005 and 3168 affected residents were finally included. FP patients were included as member of a comparison group when they were not identified as affected resident (see above), so that we could relate our findings to normal fluctuations in utilization rate and morbidity over time. The comparison group were patients in the same practices involved in our study and they had to have been registered throughout the study period. They were matched with the affected residents on gender, age and health insurance, variables which were extracted from the FPs' electronic medical records (EMR). The type of health insurance was used as a proxy for socio-economic status (SES), because this is directly related to income in the Netherlands. Persons with public health insurance are presumed to belong to a low or medium SES category and they make up 64% of the general population [21]. Private health insurance indicates a high SES.

Groups of female and male affected residents were made and five age groups were constructed. The limits of the age groups were chosen on the basis of research in Dutch family practice [21, 22]. Children younger than five years of age were not included.

Dependent variables

The International Classification of Primary Care (ICPC), which is used in Dutch family practice, is compatible with the International Classification of Diseases (ICD-10) and with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IIIR) [23]. ICPC is a multi-axial classification system in which it is possible to register problems and symptoms in the words of the patient ('the Reason for Encounter') as well as the diagnoses as objectivised by the family practitioner. Symptoms and diagnoses registered in the EMR during contacts with patients were extracted for this study every three months and were grouped in one psychological and two physical clusters (musculoskeletal and digestive) in accordance with the ICPC. The choice of these clusters was based on the results of other studies in this population demonstrating a relationship with the disaster [24-26]. The cluster of the psychological problems consisted of ICPC codes representing stress reactions, anxiety and depressive problems/disorders. The most prevalent ICPC codes within the pre – disaster psychological cluster represented depressive disorder, sleeping problems, anxious feelings and depressed feelings (constituting 64% of the cluster). By clustering problems and disorders specific information was lost, but we prevent coincidental differences between gender and age groups due to limited numbers. In the ICPC no specific code exists for PTSD. There is one code for all stress reactions, acute, transient as well as PTSD.

Statistical analysis

The study period started one year before the disaster and lasted until five years post-disaster. Utilization of family practice care was calculated as the number of contacts (consultations, visits and telephone contacts) per patient – affected residents and members of the comparison group – in six one-year periods. A dummy variable was created with yes (= 1, at least one contact in a one-year period) and no (= 0, no contact in a one-year period). Morbidity of health problems in the three clusters was calculated as the number of affected residents attending their FPs with those problems.

Differences and trends in average utilization rate and percentage of morbidity for each group (combinations of affected residents and members of the comparison group with gender or age categories) in different years were calculated and tested using a logistic multilevel model for repeated measures (using the MLwiN software) and the logistic estimation was performed with second order penalized quasi-likelihood (PQL) approach with unconstrained level 1 variance, which made it possible to control for the autocorrelation between measurements in individuals (modelling the full variance/covariance matrix between measurement occasions at person level). The person cluster in the practices was also controlled for, by using the FPs as a higher level in the model. Our research questions are specified as a linear contrast function that captures the relevant changes between post-disaster versus pre-disaster years within one group of affected residents, compared to the referenced group of affected residents. It was subsequently tested whether the difference between these internal group changes differed from zero.

Ethical approval: in accordance with the privacy protection procedures of the Dutch Data Protection Authority.

Results

The groups of affected residents and matched comparisons both contained 3164 persons, 52% of which were men (table 1). There were more women in the youngest groups and in the oldest groups (5–14 and 65+).

Gender

Utilization rates

Utilization rate was monitored during one pre-disaster year and five post-disaster years. Female affected residents and comparisons already had a higher utilization than male affected residents and comparisons before the disaster occurred. Both female and male affected residents had a significant post-disaster increase (table 2) in the first year ($P < .001$) compared to pre-disaster. The second year again showed a statistically significant difference in both female ($P < .001$) and male affected residents ($P < .01$). When the increases in the utilization rates for female and male affected residents were tested in the first two years, a significant difference ($P < .01$) was found in the second year alone, which means that the increase in utilization rate remained significantly higher in female affected residents. The increase in the first year was similar for both sexes.

Psychological problems

Psychological problems were analyzed per gender during the same period. Female affected residents had higher levels of psychological problems than males during the overall study period, including the pre-disaster period (table 3), and both groups of affected residents showed a statistically significant increase in these problems ($P < .001$) in the first post-disaster year. The psychological problems decreased moderately after the first year post-disaster. The difference with the pre-disaster year remained significant until the fourth year for men and until the third year for women. When the differences between the increases for men and women were tested, however, they did not appear to be significant, which meant that the increased morbidity of psychological problems post-disaster was similar for men and women, given the existing pre-disaster differences.

Table 1. Numbers of male and female affected residents registered with a family practice in a period of one year predisaster and five years post-disaster

Age group in years	Male	Female
5–14	150	160
15–24	202	176
25–44	624	532
45–64	508	394
65+	156	262

Physical symptoms

No statistically significant increases were found in male and female affected residents when changes in musculoskeletal and digestive symptoms were compared between the pre-disaster year and the five post-disaster years. Nor were any significant differences found between the changes in both sexes (table 3).

Age

Utilization rates

Utilization rates in five post-disaster years were compared with the pre-disaster year. The tests were implemented for all affected residents in five age groups and related to the comparison group (table 4). All age groups demonstrated a statistically significant increase in the first post-disaster year (5–14 years $P < .05$, all other groups $P < .001$) and this increase persisted in the second year in some groups (25–44 years, $P < .001$ and 44–65 years, $P < .01$) and even in the third year (25–44 years, $P < .05$). These increases in each age group were compared with the adjoining older group and with the mean of all older groups, but no significant differences were found in the changes between the pre-disaster year and the post-disaster year in all age groups.

Psychological problems

Psychological problems in the post-disaster years were compared with those in the pre-disaster year and a statistically significant increase in psychological problems was found in all five age groups in the first year ($P < .001$, table 5). These significant differences persisted in the adult groups and in the elderly in the second year (25–44 years ($P < .001$), 45–64 years ($P < .001$), 65+ ($P < .01$)) and in the third year (25–44 years ($P < .001$), 45–64 years ($P < .001$), 65+ $< .05$)). A statistically significant difference was finally found in the adult group of 25–44 years in the fifth year ($P < .001$). No significant differences were found between the pre/post increases in all age groups.

Physical symptoms

No statistically significant differences were found in the first year post-disaster when the post-disaster musculoskeletal and digestive symptoms of five age groups were compared with their pre-disaster levels. Again, no significant differences were found when all age groups were compared with their adjacent older age groups.

Table 2. Utilization rate by male and female affected residents and members of the comparison group as number of contacts with FPs per year, one year pre-disaster and five years post-disaster

Utilization rate		Male		Female	
		affected	comparison	affected	comparison
Pre-disaster	Year 0	3, 69	3, 06	6, 61	5, 44
Post-disaster	Year 1	5, 21***	3, 25	8, 51***	5, 63
	Year 2	4, 73**	3, 34	8, 38***§	6, 06
	Year 3	4, 81	4, 13	8, 60	6, 98
	Year 4	4, 48	4, 16	8, 17	7, 30
	Year 5	4, 53	4, 12	7, 88	6, 59

** $P < .01$, year compared with year 0

*** $P < .001$, year compared with year 0

§ $P < .01$, women compared with men within one year and related to year 0

Table 3. Psychological, musculoskeletal and digestive symptoms in percentages of male and female affected residents and members of the comparison group attending their FP at least once per year, one year pre-disaster (year 0) and five years post-disaster (years 1 through 5)

Psychological symptoms		Male		Female	
		affected	comparison	affected	comparison
Pre-disaster	year 0	12, 9	10, 9	19, 1	14, 9
Post-disaster	year 1	40, 8***	11, 5	55, 1***	18, 4
	year 2	24, 6***	12, 8	33, 5***	16, 9
	year 3	24, 0***	13, 7	33, 4**	20, 4
	year 4	19, 0*	12, 7	28, 8	20, 8
	year 5	16, 9	13, 2	24, 3	17, 3
Musculoskeletal symptoms		Male		Female	
		affected	comparison	affected	comparison
Pre-disaster	year 0	23, 0	19, 8	29, 1	23, 9
Post-disaster	year 1	25, 4	19, 8	31, 1	24, 2
	year 2	22, 8	18, 8	30, 7	24, 8
	year 3	22, 2	19, 6	31, 3	24, 4
	year 4	20, 1	19, 4	27, 1	24, 4
	year 5	20, 7	17, 7	28, 5	23, 6
Digestive symptoms		Male		Female	
		affected	comparison	affected	comparison
Pre-disaster	year 0	12, 2	10, 1	14, 9	14, 1
Post-disaster	year 1	12, 9	9, 4	18, 1	14, 3
	year 2	11, 9	9, 6	16, 6	13, 3
	year 3	12, 9	10, 4	16, 8	14, 6
	year 4	13, 2	11, 7	18, 7	15, 4
	year 5	11, 5	11, 3	16, 6	14, 7

* P < .05, year compared with year 0
** P < .01, year compared with year 0
*** P < .001, year compared with year 0

Table 4. Utilization rate by five age groups of affected residents and members of the comparison group as mean number of contacts with FPs per year, one year pre-disaster (year 0) and five years post-disaster (years 1 through 5)

Utilization rate		Age groups									
		Age 5–14		Age 15–24		Age 25–44		Age 45–64		Age 65+	
		A	C	A	C	A	C	A	C	A	C
Pre-disaster	Year 0	0, 97	1, 61	3, 20	2, 42	4, 51	3, 48	6, 51	5, 19	9, 44	9, 28
Post-disaster	Year 1	1, 69*	1, 58	4, 79***	2, 46	6, 54***	3, 36	8, 19***	5, 84	11, 12***	9, 66
	Year 2	1, 48	1, 77	3, 73	2, 78	6, 20***	3, 67	8, 19**	5, 98	10, 80	9, 99
	Year 3	1, 42	2, 06	3, 91	3, 22	5, 86*	4, 12	8, 30	6, 76	12, 54	12, 88
	Year 4	1, 45	1, 97	3, 05	2, 91	5, 34	4, 43	8, 13	7, 23	12, 23	12, 66
	Year 5	1, 55	1, 74	3, 05	2, 65	4, 84	4, 03	8, 35	6, 77	12, 17	12, 43

A Affected residents
C Comparison group
* P < .05, year compared with year 0
** P < .01, year compared with year 0
*** P < .001, year compared with year 0

Discussion

The aim of this study was to explore whether female affected residents were more vulnerable than male ones and whether younger age groups were more vulnerable than older groups to the effects of a man-made disaster in a longitudinal design with a pre-disaster measurement and a comparison group. Changes in service utilization and in morbidity as presented by patients in family practice were tested.

The main finding of the study is that no statistically significant differences were found between men and women and between various age-groups with regard to post-disaster increases in utilization rate, in psychological problems and in physical symptoms. We conclude, therefore, that as such, female gender and younger age were no risk factor in family practice following this disaster. The finding that women present a higher utilization than men in the second year alone was an unexpected one. It is hard to explain, because no gender differences in presenting with psychological problems were found in the same year.

This finding that female gender is not a risk factor after a disaster is in contrast with the findings of many other studies [1-7, 27]. A difference between our study and previous studies on gender differences may be that the previous studies were often based on natural disasters with a sudden and fierce impact, e.g. earthquakes or hurricanes. Such disasters may cause more extensive destruction of housing and infrastructure than the man-made disaster in the present study and these large scale disasters may have an additional impact on women as breadwinners, having to raise children, or losing social support [11].

Some studies on gender, however, demonstrated results resembling those in our study. In a study on gender effects after 9/11 [28], a lifetime risk of post-traumatic stress disorder (PTSD) in women was found that showed that PTSD was not directly related to the attacks. In another study on 9/11, an excess burden of PTSD was attributed to female behavioural factors (e.g. acting as primary caregiver, experience of peri-event panic attacks) and biographical factors (e.g. previous unwanted sexual contact, recent history of mental problems) [29]. The disaster itself seemed to play a limited role in these studies. Another study concerning the effect of an air show disaster showed that gender did not act as a risk factor on post-traumatic stress symptoms [30]. These three studies were controlled for pre-disaster morbidity. One 9/11 study about female victims without a pre-disaster assessment found a relationship between social and economic circumstances and PTSD suggesting that women are not more vulnerable to PTSD than men [31].

Table 5. Psychological morbidity in percentage of five age groups of affected residents and members of the comparison group visiting their FP at least once per year, one year pre-disaster (year 0) and five years post-disaster (year 1 through 5)

Psychological problems	Age groups								
	Age 5–14		Age 15–24		Age 25–44		Age 45–64		Age 65+
	A	C	A	C	A	C	A	C	AC
Pre-disaster Year 0	6, 2	7, 1	12, 2	8, 7	17, 9	12, 6	18, 4	14, 8	16, 4 19, 0
Post-disaster Year 1	25, 6***	5, 2	41, 2***	10, 4	49, 9***	15, 6	53, 9***	17, 5	51, 4*** 20, 4
Year 2	14, 0	7, 4	22, 2	11, 2	31, 9***	15, 5	33, 8***	17, 3	28, 0** 18, 3
Year 3	13, 0	8, 9	25, 8	15, 0	30, 8**	16, 3	31, 0**	18, 5	31, 5* 25, 0
Year 4	12, 4	7, 4	19, 4	12, 7	25, 9	17, 0	26, 3	18, 8	25, 2 23, 4
Year 5	8, 4	6, 1	18, 1	10, 9	22, 5***	16, 2	23, 0	16, 3	21, 5 22, 7

A Affected residents
C Comparison group
* P < .05, year compared with year 0
** P < .01, year compared with year 0
*** P < .001, year compared with year 0

After studying reviews and meta-analyses [1, 10, 11] we concluded that results of studies about gender being a risk factor for post-disaster utilization and morbidity (or not) were influenced by the study design. Retrospective studies were associated with weaker effects for female gender and the effect size was greater when respondents were interviewed rather than given questionnaires[10]. Epidemiological studies were associated with a significantly greater sex difference in PTSD than were convenience-sample studies [11]. Our design was not retrospective, no respondents were used (no 'recall bias') and epidemiological methods were applied. Based on the literature mentioned we hypothesized (strong) effects for women, although our study did not concern PTSD, but stress reactions, depressive feelings/disorders and anxiety feelings/ disorders and physical symptoms. Moreover, the effect of demographic characteristics can not be thoroughly understood without controlling exposure and/or subjective appraisal characteristics. As mentioned before, privacy rules made it impossible to be 100% certain about the amount of exposure and subjective characteristics were not available because existing registries were used.

In our study, all five separate age groups presented postdisaster increases in psychological problems and utilization. These increases did not differ from one another, however, and so it appeared that all age groups were equally vulnerable to the effects of the disaster. This is in contrast with the finding of Norris in her review, which was that 88% of all studies of adult victims showed that younger adults were more adversely affected by disaster than older adults [1]. We found no results, therefore, to support the inoculation theory as presented in several studies showing a stronger resilience of elderly victims to the effects of a disaster [14-16]. In contrast to the present study, however, these studies were performed after natural disasters and two of them included high proportions of older adults [14, 15]. High age elderly were compared with young age elderly, but these groups were pooled in one 65+ group in our study, because of the low numbers of victims in these groups. One of the flood studies was controlled for pre-disaster morbidity[15]. Age was studied in an adult group of victims in the study of an air show disaster referred to above, which was controlled for pre-disaster symptoms. Like gender, age did not appear to be a risk factor for post-disaster psychological problems in this study [30].

In summary, gender and (younger) age as such are not risk factors for presentation of post-disaster utilization or morbidity in the present study. Of the few studies that confirm our findings, two had a "pre-disaster" design similar to our study [15, 30]. The studies that showed female gender and younger age to be risk factors were mostly based on large scale natural disasters and they did not perform predisaster assessments and or used a comparison group.

Limitations and strengths

The present study has a strong design with pre-disaster data being used as a baseline measurement; as Norris stated in her review [1]: 'controlling for pre-disaster symptoms when assessing the effects of exposure yields the strongest design possible in this field of research'. As a consequence, we already had insight into pre-disaster health problems and the results of our study could be controlled for pre-disaster baseline values. Health data of affected residents and comparisons were also compared and a risk of recall bias was avoided as well by using FPs' electronic medical records instead of self-reported questionnaires.

Some issues relating to the present study need to be considered. Differences between affected residents and the comparison group already existed before the disaster occurred and affected residents presented more psychological and physical problems, in spite of matching with controls on socio-economic status, gender and age. Adverse health outcomes in the aftermath of disasters often originate in poor social circumstances that already existed before the disaster. In addition,

disasters tend to happen in socially deprived areas with residents presenting more health problems or in areas that are particularly vulnerable to the effects of natural disasters [32, 33]. On the other hand, the type of health insurance turned out to be an insufficient proxy for the socio-economic status of affected residents and members of the comparison group.

In this study, we did not have any information about whether the affected residents were directly exposed or not. We are aware that this is an opportunistic study which was limited by practical problems often encountered in disaster research. In this case, due to privacy regulations it was not possible to explore the 'individual exposure'. To overcome this problem two external sources were used: persons were either marked as affected in the patient registration of their FP (using the zip-codes of the affected area or because being affected was mentioned in the patient – practitioner encounter), or were registered in the database of the municipal Information and Advice Centre (IAC); residents were for example registered here for acquiring a new house and for financial compensation. Indirectly, there is evidence that affected residents were directly exposed to the disaster. After this disaster, besides surveillance in family practice, a survey was conducted using questionnaires. It was possible to combine the two databases (questionnaires and EMRs from family practice) for 994 affected residents (31.5% of the study group used here). On average, these persons reported 10.4 stressful experiences during the disaster (e.g. saw smoke, heard the explosions, saw the explosions, felt the shockwave, saw dead bodies) and analyses of SCL-90-R subscales and Rand-36 subscales showed that having encountered stressful experiences during the disaster was significantly associated with more problems on all subscales [34]. In another study on 649 affected residents (20% of our study group), 75% of them had high scores (>25) on the Impact of Event Scale [35]. These results were not confirmed in the comparison group. Finally, in a secondary analysis, it was found that prevalence rates of the comparison group resembled those of the general Dutch population, while the affected residents had higher rates on several health problems [36].

We may conclude that indirect evidence confirms that the labelling of the study groups reflects a distinction between individual exposure among the affected residents and no exposure among members of the comparison group.

Psychological problems were combined in one cluster, which might have resulted in loss of specific information. The choice of clustering patient's problems was decided in order to prevent coincidental differences due to the limited numbers of patients. On the other hand, symptoms of PTSD, anxiety disorder and major depression, which are all co-morbid with each other, were included in the cluster.

A risk of overrepresentation of post-disaster psychological problems could not be excluded. After all, the FPs in the study knew their patients and who was an affected resident and who was not. On the other hand, they knew whether a problem that was attributed by the affected resident to the disaster, was presented in reality before the disaster as well [32]. Moreover, recall bias could be avoided by the use of EMRs. Finally, the FPs were trained in the ICPC classification system and they received feedback on the quality of their registrations.

Conclusion

In conclusion, the fireworks disaster appears to have dispersed its impact equally among male and female affected residents of all ages. In specific terms, neither women nor any particular age group were at increased risk of suffering the detrimental health effects of this man-made disaster in a residential area. In other studies concerning this specific disaster, it was found that having a pre-disaster history of psychological problems and disorders appeared to be the most important risk factor for post-disaster psychological as well as physical health problems [24-26]. In the first three years post-disaster be-

ing relocated due to the disaster appeared to be another strong indicator for disaster related health problems. Risk factors which appear in 'normal' primary care (gender, age, insurance type, ethnicity) did not have any extra effect of the disaster: post-disaster differences between these groups may be explained by pre-disaster differences.

After disasters family practitioners do not have to focus specifically on gender or on any age group post-disaster, but especially on those with psychological problems before the disaster and patients who lost their houses and personal belongings. As Freedy mentioned [37], after disaster 'family practitioners are key agents for providing information, remaining empathic, encouraging patients to seek and accept assistance (...) and repeatedly checking on disaster victims for up to (at least) 12 months'

Our study is one of the first which used a pre-post design and a longitudinal control-comparison design, using existing registries in family practice. It is important that this alternative design will be implemented after another disaster, collecting exposure data as well.

Authors' contributions

RJHS originated and wrote the article, and assisted with the analysis. CJY supervised all aspects of the study. PS completed the analysis. TALML-J, WJHMvdB and JvdZ originated the study and provided feedback and suggestions throughout. All authors helped to develop ideas, interpret findings and review drafts of the manuscript.

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TESTING FOR ALLERGIC DISEASE: PARAMETERS CONSIDERED AND TEST VALUE

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Background: Test results for allergic disease are especially valuable to allergists and family physicians for clinical evaluation, decisions to treat, and to determine needs for referral.
Methods: This study used a repeated measures design (conjoint analysis) to examine trade offs among clinical parameters that influence the decision of family physicians to use specific IgE blood testing as a diagnostic aid for patients suspected of having allergic rhinitis. Data were extracted from a random sample of 50 family physicians in the Southeastern United States. Physicians evaluated 11 patient profiles containing four clinical parameters: symptom severity (low, medium, high), symptom length (5, 10, 20 years), family history (both parents, mother, neither), and medication use (prescribed antihistamines, nasal spray, over-the-counter medications). Decision to recommend specific IgE testing was elicited as a "yes" or "no" response. Perceived value of specific IgE blood testing was evaluated according to usefulness as a diagnostic tool compared to skin testing, and not testing.
Results: The highest odds ratios (OR) associated with decisions to test for allergic rhinitis were obtained for symptom severity (OR, 12.11; 95%CI, 7.1–20.7) and length of symptoms (OR, 1.46; 95%CI, 0.96–2.2) with family history having significant influence in the decision. A moderately positive association between testing issues and testing value was revealed ($\beta = 0.624$, $t = 5.296$, $p \leq 0.001$) with 39% of the variance explained by the regression model.
Conclusion: The most important parameters considered when testing for allergic rhinitis relate to symptom severity, length of symptoms, and family history. Family physicians recognize that specific IgE blood testing is valuable to their practice.

Background

With the prevalence of allergic rhinitis estimated at 21% – 23% for the European population and 20% – 40% for the western population, appropriate diagnosis and treatment of allergic rhinitis is of global importance [1, 2]. Family physicians are usually first approached by patients experiencing symptoms; however, little information exists regarding the rationale to perform specific IgE blood testing, which parameters are most important, and the value of such testing. Given the need to determine if symptoms are truly attributed to allergic mechanisms, it is important that family physicians consider diagnostic testing in conjunction with a careful examination of patient history, clinical evidence, and environmental exposure factors to optimize patient care. The consequences of untreated symptoms can lead to multiple future complications while the consequences of misdiagnosis can lead to inappropriate treatments [3].

Chronic rhinitis has detrimental effects on quality of life and work productivity [4, 5]. Although medications may control symptoms in some patients, it is difficult to distinguish between allergic rhinitis and non-allergic rhinitis using clinical evaluation and medication trials. Two commonly applied methods are used to uncover an allergic etiology and identify possible causes. These include skin prick tests (SPT), and specific IgE tests that are thought to produce concordant measures on a dichotomous basis for specificity and sensitivity, as well as a propensity toward appropriate diagnoses in relation to the presence of specific IgE antibody levels [6, 7]. Decisions to utilize these tests are influenced by experience, patient history, diagnostic accuracy and efficacy of the test, and how well test results relate to symptoms [8, 9].

When presented with patient complaints and bothersome symptoms that may or may not be related to allergic rhinitis, phy-

sicians rely on numerous strategies to make an appropriate diagnosis. How family physicians weigh the importance of these patient-related parameters when recommending specific IgE testing is largely unknown, yet instrumental to determine appropriate treatment and follow-up therapy. To address this research question, we used a trade off approach (conjoint analysis) to evaluate family physicians' preference to recommend specific IgE blood testing with respect to patient symptoms, family history, and medication use. A second approach using visual analog scaling (VAS) was added to validate and compare findings obtained from the conjoint analysis. Visual analog scales have been used extensively in clinical assessment to quantify patient perceptions of disease severity and the impact of symptoms on health [10, 11]. Further evaluation was performed to determine if family physicians perceive that testing, as part of the care process was valuable to patient care. As healthcare gatekeepers, family physicians have the best opportunity to construct a baseline assessment of these patients to determine if current treatment strategies are effective, or if patients would benefit from a referral to an allergist or other specialist.

Methods *Study sample*

Primary care (family) physicians in a southeastern state in the United States were identified through already established medical societies and physician mailing lists that

were complied at the Recruitment and Retention Shared Facility at the University of Alabama, Birmingham. Mailing addresses, telephone numbers, fax numbers, specialty area, and practice affiliation was verified for 424 physicians in Alabama. From the list of 424 physicians, a sample of 150 physicians was randomly selected to participate in the study. Three separate mailings containing 50 questionnaires were sent by priority mail, one week apart to these physicians at their respective practice sites. The questionnaire package contained a letter of invitation to participate in the study, along with a self-addressed stamped envelope for the returned questionnaire. Thirty-two questionnaires were completed and returned during the first month, follow-up reminder calls were conducted three weeks after the initial mailing (77 calls were answered), and 14 surveys were faxed per request by providers. A total of fifty completed surveys were returned within two months. The estimated sample size of 50 was determined for this study following examples for studies with repeated-measures designs [12]. As an incentive, a gift certificate for a local department store was mailed to physicians who completed the questionnaire.

Instrument Development

Techniques to evaluate preference include standard gamble, alternate rating (e.g., visual analog) scale, and time trade-off [13]. Besides these techniques, conjoint analysis (a trade off approach among attributes) is another technique that is used to evaluate the importance of preference measurements [14]. Choices are usually presented in the form of profiles that are ranked or rated (e.g., recommend specific IgE testing – yes or no). The part-worth values (coefficients) for each attribute are obtained from the random effects logistic regression model analysis with repeated measures (50 responses Ч 9 profiles = 450 observations), which follows stated choice experiments based on choice theory [15, 16]. Although developed in marketing research, the use of conjoint analysis in health care is becoming a valuable tool [17-20].

In an attempt to simplify the conjoint exercise for this study, each attribute was assigned three levels (see Additional file 1). For example, symptom severity was assigned "high, " "medium, " or "low, " and symptom length appeared as symptoms for "less than 5 years, " "symptoms for 10 years, " and "symptoms for more than 20 years." Family history included "neither parent has allergic rhinitis, " "mother has allergic rhinitis, " and "both parents have allergic rhinitis." Medication use included the use of "over-the-counter medications to control allergy symptoms, " "prescribed antihistamines, " and the "pre-

scribed nasal spray to control allergy symptoms." Effects coding was used to construct the numerical values of the profile attributes. The "low" level was the reference value and was denoted as -1. The "high" level was denoted as +1.

A one-third fractional factorial design using repeated measures was chosen to minimize the number of profiles to 9 thereby attempting to avoid respondent fatigue. Two additional profiles were produced manually as holdout profiles for use in validation [21]. Each profile portrayed an individual with a pre-determined set of allergic symptoms and clinical indicators. For the dependent variable, family physicians were asked to provide a "yes" or "no" response to whether they would recommend specific IgE blood testing for this patient. For the purposes of this study, which specific IgE blood test was used by family physicians was not important, or what type of test (food or inhalant) was performed.

The hypothesis for this study was that the estimated partworth values or coefficients, exponentiated to odds ratios in this study, for each of the four profile attributes were simultaneously equal to zero. In the next section, family physicians were asked to indicate if recommendations to test were influenced by managed care guidelines, value of testing, referral activities, familiarity with specific IgE testing, relation of test results to symptoms, and value of test to practice, the likelihood to use specific IgE testing using a ten-point scale "less likely to test" to "more likely to test." Specific IgE blood testing was rated using a scale ('1' = not valuable to '6' highly valuable) for overall value, value compared to skin testing, and value compared to not testing at all. Demographic characteristics of participating family physicians, such as age, gender, years in practice, and practice site information, were elicited in the last section of the questionnaire. To assess questionnaire validity, participants provided an estimate of a patient's overall health status given the impact of various symptoms and clinical indicators with 0 being the "Worst Possible State" and 100 being the "Best Possible State." The means for these items were compared to those rankings obtained from the conjoint exercise to offer additional information regarding testing.

Data analysis

Descriptive statistics were provided for demographic variables. The conjoint exercise data were analyzed using a random effects logistic regression model. This type of model was chosen since it produces standard errors that account for the intra-individual correlation. Assumptions of normality, linearity, and equal variances among the items were evaluated to ensure appropriate interpretation of statistical analyses. All statistical analyses were performed using Stata/SE version 9 (College Station, Texas, USA). An Institutional Review Board from the University of Alabama, Birmingham, granted approval for the study.

Results *Demographics*

Participating physicians (33% response rate) were more likely to be male, between 40 and 60 years of age and with about 20 years of clinical experience in a private practice setting (Table 1). Independent *t*-test revealed that among older physicians (> 50 years), those with 10 or more years in practice placed a greater value on specific IgE testing than not testing (n = 32; mean = 4.6) compared to those with less than 10 years in practice (n = 18; mean = 3.8; t = 2.2; P = 0.03).

Conjoint model

Results from the random effects logistic regression model are presented in Table 2. The interaction between study attributes and demographic characteristics was not significant. Attributes, that are more likely to influence decision to request specific IgE blood testing, were symptom severity, length of time having symptoms, and history for allergic rhinitis reported for both parents. Results reveal the log likelihood = -196.983, Wald χ^2 = 94.03, P < 0.0001, with 448 observations for 50 physicians each physician evaluating 9 profiles, thus supporting the hypothesis that the impact of parameters on specific IgE

blood testing are not perceived equally. Symptom severity had the greatest impact on physician decisions to test patients for allergic rhinitis (OR, 12.11; 95%CI, 7.1–20.7). Thus, one would expect that physicians would be 12 times more likely to consider the specific IgE blood test for patients with high symptom severity compared to patients with low symptom severity. Although not significant, other attributes such as length of symptoms and both parents having a history of allergic rhinitis influenced physician decisions to test (OR, 1.46; 95%CI, 0.96–2.2: OR, 1.44; CI, 0.95– 2.2, respectively). However, some physicians may not be willing to trade among the alternatives when the decision involved a potentially dominant attribute, where symptom severity may be the only reason to recommend specific IgE blood testing. To assess the potentially dominant effect of symptom severity [22], two versions of the model were run – one containing profiles where symptom severity was present and one containing only those where symptom severity was absent (results not shown). In both situations, other parameter estimates were significant indicating the hypothesis that coefficients were simultaneously equal to zero was rejected regardless of the presence of the symptom severity.

Table 1. Demographic Characteristics of Family Physicians

Characteristic	Value (n = 50)
Age, y	
Mean (SD)	49 (12.0)
Range	29 – 79
Years in Practice	
Mean (SD)	18.6 (12.4)
Range	2 – 52
Gender, no. (%)	
Male	35 (71.4)
Female	14 (28.6)
Practice type, no. (%)	
Private/Independent	43 (87.8)
Managed care setting	6 (12.2)

Table 2. Results from the random effects logistic regression model

Attribute	Level	Odds Ratio	P-value	95% CI
Symptom severity	High	12.11	<0.001[a]	[7.1, 20.7]
	Medium	1.46	0.281	[0.84, 1.9]
	Low*	0.06		
Length of symptoms	>20 years	1.46	0.073[b]	[0.96, 2.2]
	5 years to 20 years	1.39	0.074[b]	[0.96, 2.2]
	<5 years*	0.47		
History of allergic rhinitis	Both parents	1.44	0.089[b]	[0.95, 2.2]
	Mother only	1.20	0.37	[0.80, 1.8]
	Neither parent*	0.58		
Medication use	Intranasal corticosteroids	1.12	0.586	[0.75, 1.7]
	Prescribed antihistamines	1.33	0.171	[0.89, 2.0]
	OTC allergy medications*	0.67		

Validation

Two methods were used to validate the results of the conjoint exercise – the use of a holdout profile and an alternate rating method. First, was to estimate predictive validity for the holdout profile using the regression model developed from the 9 orthogonal profiles. The relation between the observed response for the holdout profiles and the predicted responses was then examined. The predicted values for the holdout profiles were quite similar to the observed value. The predicted mean probabilities were 82.7% and 78.4% compared to the observed values 70% and 78%, respectively. The differences were not significantly different (*t*-test; $p = 0.162$, $p = 0.996$, respectively) suggesting that the conjoint model exhibits acceptable internal predictive validity. Second, was the use of a VAS where participants responded to each item from the conjoint study presented separately. Lower mean scores obtained for each

domain indicated that the particular domain represented choices that were less desirable to the respondent. Symptom severity (mean = 36.7; SD = 16.4) and symptom length (mean – 36.0; SD = 16.6) were ranked the worst followed by medication use (52.6; SD = 21.5), and family history (mean = 61.0; SD = 24.0), revealing consistent response patterns between the conjoint study and the VAS.

Impact of testing issues on value

Kaiser-Meyer-Olkin measure of sampling adequacy for the final principal components analysis was 0.82 and the significant ($p \leq 0.001$) Bartlett test of sphericity supported the use of factor analysis for the items used to assess testing issues [23]. One factor was retained for testing issues accounting for 54.6% of the variance. Two items, difficulty in interpreting test results and insurance coverage were dropped from the analysis. The factor structure was further verified by reanalyzing the reliability of the dimension. Descriptive statistics (item's mean and standard deviation) and Cronbach's alpha for study items are presented in Table 3. Most noteworthy, was that physicians perceived that "how well the test correlated with symptoms" was given the highest score (mean = 7.6; SD = 1.9) with respect to "more likely to use specific IgE testing." In addition, physicians perceived that specific IgE testing had significant ($p \leq 0.007$) value overall, perceived value compared to not testing, and perceived value was comparable to skin testing. Cronbach's alpha for the remaining nine items for testing issues was 0.90 and 0.86 for the three items consisting of testing value, indicating a high degree of internal consistency or a high signal-to-noise ratio (i.e., error variance minimized) across individuals [24].

Linear regression analysis was used to assess the relationship between testing issues and testing value. As hypothesized, results using composite scores for testing issues and testing value revealed a moderately positive association between these two dimensions ($\beta = 0.624$, $t = 5.296$, $p \leq 0.001$) with ($R^2 = 0.39$) 39% of the variance explained by the model.

Discussion

According to our results, family physicians consider symptom severity to be the significant determinant, followed by symptom length and family history when recommending the use of specific IgE blood testing for patients suspected of having allergic rhinitis. Physicians in practice for 10 years or more placed greater value on specific IgE testing compared to those in practice for less than ten years. Moreover, results from VAS were consistent with findings from the conjoint study. Our findings were also corroborated in another recent study where VAS for symptom severity compared favorably with standard quality of life measures [25].

Table 3. Descriptive Statistics and Scale Evaluation for Issues and Test Value

	Mean (SD)
Testing issues *	
Managed care practice guidelines	5.4 (2.3)
Patient's perceived value of the test	6.5 (1.9)
Reduced need to refer patients to allergists	6.8 (2.0)
Difficulty in interpreting test results	4.4 (2.6)
Familiarity with test use	6.9 (2.3)
Patient demand to have the test done	7.0 (1.9)
Type of allergic rhinitis (intermittent vs. persistent)	6.6 (1.9)
How well test results relate to symptoms	7.6 (1.9)
Value of testing to my practice	6.9 (2.3)
Testing value **	
Overall value of specific IgE as a diagnostic tool	3.9 (1.1)
Compared to skin testing, usefulness of specific IgE blood testing	3.9 (1.4)
Compared to not testing at all, usefulness of specific IgE blood testing	4.3 (1.2)

Professional organizations such as the American Academy of Allergy, Asthma, and Immunology and the European Academy of Allergology and Clinical Immunology recognize that allergic disease is a major health concern often requiring specific allergen avoidance and treatment strategies that are based on positive findings from history and diagnostic testing [26, 27]. Results from this study support the positions elicited from the Joint Task Force on Practice Parameters for Rhinitis and Allergic Rhinitis and its Impact on Asthma (ARIA) in that family physicians are capable of recommending specific IgE testing, using the test to confirm allergic disease and identifying possible allergens [28-30]. Also consistent with recommendations from the Joint Task Force, results from the VAS closely approximated the findings of the conjoint study, thus revealing the usefulness of VAS in clinical practice to assess symptom severity for patients suspected of having allergic rhinitis.

Values for each item relating to patient perceptions of the test, patient demand to have testing performed, other clinical indicators, and the type of allergic rhinitis were summated to create a composite score. This composite score for testing issues yielded a moderately positive correlation with testing value, thus providing initial evidence that issues associated with testing and the process of care were linked to outcomes such as testing value. Moreover, positively framing the information describing the benefits of

testing and the value of testing to patients is also known to influence their expectations of benefits [31].

Limitations include a low response rate and a cross-sectional study representing one geographical region. In addition, family physicians may consider attributes that were not evaluated in this study when deciding to request specific IgE blood testing for patients suspected of having allergic rhinitis. Hypothetical profiles were developed for this study and may not include all aspects of information provided by patients to family physicians, reflect what happens in actual clinical practice, and represent the opinions of physicians in other geographical areas.

Given the economic burden of allergic rhinitis on society and the research evidence that supports an inverse relationship between health status and specific IgE antibody levels [32-34], current guidelines should be repositioned and possibly modified to allow family physicians to have a more active role in specific IgE blood testing. Although ARIA suggests the SPT as a first line choice when further evaluation of patients is needed, interpretation of test results requires extensive training and experience. Thus, specific IgE testing was examined in this study as a practical choice for primary care physicians. As suggested from this study and supported in the literature, with proper training family physicians would become more adept at quantifying the results from specific IgE blood testing and recognizing when to refer patients (e.g., continued treatment failure, complications, and beyond scope of expertise) to allergists or other specialists [35-38]. Another important aspect of training is the need to consider specific IgE blood test and SPT results in the context of patient history, especially when discrepancy exists between test results and symptoms. Diagnostic testing, *per se*, is no substitute for a thorough examination of patient symptoms, health status, and medical history. In summary, allergists and family physicians understand that test results coupled with the findings of a careful clinical examination serve as the foundation to establish a strategy for treatment, from which future health outcomes can be evaluated to determine the success of treatment.

Conclusion

Family physicians rely on symptom severity, and to some extent on length of time that symptoms are present and family history to determine whether patients should be tested to determine the presence of allergic disease. Physicians with more practice experience placed greater value on specific IgE testing. Findings also revealed a moderately positive association between the issues influencing the use of specific IgE blood testing

and test value. Overall, family physicians valued specific IgE blood testing, especially compared to not testing.

From the study findings, family physicians can use symptom severity as a gauge in clinical practice to determine if patients should undergo detection and testing for allergic rhinitis or related conditions perhaps much earlier during the process of clinical evaluation, especially in the presence of severe symptoms and a positive family history. Baseline evaluation will also increase the likelihood of determining the correct diagnosis and appropriate treatment, and to ascertain the need for referral. Future research is needed to address the impact of patient expectations and treatment experience on value and other outcome measures.

Authors' contributions

SLS conceptualized the study, examined the study design, performed the statistical analysis, and drafted the manuscript. SEH setup the study design, performed the statistical analysis, and drafted the manuscript. PBW conceptualized the study, examined the study design, and provided a critical assessment of the manuscript. HE coordinated and managed the collection of data for the study and reviewed the manuscript. All authors approved the manuscript.

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PERFECTION OF DIFFERENTIAL DIAGNOSTICS AND PROGNOSTICATION OF ACUTE PANCREATITIS DESTRUCTIVE FORMS COURSE

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A complex dynamic analysis of oxidative homeostasis state in patients with various forms of acute pancreatitis was carried out. It has been established that an authentic decrease of minimal chemiluminescence intensity indexes and blood serum antioxidant activity number can serve as an additional criterion of infected pancreatonecrosis early detection. The lack of the tendency for erythrocyte peroxidative resistance increase in the postoperative period in pancreatonecrosis patients testifies to a poor prognosis of the disease. The complex diagnostics perfection allows optimizing the surgical approach and reducing the number of early traumatic surgical interferences to the minimum.
Key words: diagnostics, prognostication, chemiluminescence analysis, free radical oxidation, acute pancreatitis, pancreatonecrosis.

Introduction

Over the last 30 years a world-wide tendency for acute pancreatitis case rate increase has been depicted. The basic quota of the patients is still formed by the persons of active working age, and among the causes of the disease the alcohol dependence and alimentary factors rank first.

The number of the disease destructive forms, which make up to 44%, grows everywhere. Thereat, if the total mortality for the last 10 years has a tendency to decrease, then the postoperative one, reflecting the patients' most serious category treatment results, is still calculated by double figures.

The purpose of our research has been the improvement of acute pancreatitis patients' treatment results due to the application of a new diagnostic complex based on the chemiluminescence analysis use.

Materials and methods

Under our supervision there were 160 patients with various forms of acute pancreatitis aged from 22 to 76 years old. 54 acute pancreatitis patients having received treatment in the general surgery clinical unit of the Krasnoyarsk State Medical Academy during the period of 2002-2003, their chemiluminescence kinetics features being estimated retrospectively, the ozone therapy method being not used, made the first group. The prospective research was carried out during the period of 2004-2006 and included 106 patients of the second group, the pancreatitis destructive form diagnostics and prognostication developed criteria being used for them.

The acute pancreatitis patients' examination included general clinical, laboratorial and instrumental methods. The acute pancreatitis severity was evaluated according to the scale of V.B. Krasnogorov in all the patients. The average score in the clinical groups made 4, 6±0, 31, that conformed to a severe pancreatitis. The crucial moment in the destructive pancreatitis form verification was considered a bacteriological research.

For the peroxidative homeostasis state estimation the method of iron-induced ***luminol-dependent*** chemiluminescence (CL) with the application of the biochemiluminometer БХЛ-06М was used. Erythrocytes and blood serum served as the chemiluminescence analysis object.

Results and discussing

The chemiluminescence analysis of the blood serum testified that in all the edematous pancreatitis patients an authentic 3, 14 times increase of the maximal luminous intensity (I max) with respect to the norm and considerably less manifested light-sum growth – 1, 92-fold, are recorded at their admission. The coefficient K reflecting the total antioxidant activity of the serum exceeded

the admission control indexes 1, 65 times. In the dynamics of the disease together with peroxide concentration a gradual decrease of the blood serum antioxidant potential was registered, the tg α and coefficient K decrease testifying to the fact.

In spite of the fact that antioxidant activity indexes in the edematous pancreatitis didn't differ authentically from the control ones, beginning with the third day of traditional therapy, the total blood serum oxidative activity remained high.

The highest admission chemiluminescence intensity values were registered in sterile pancreatonecrosis patients. The level I max exceeded the age norms indexes 7-fold within the first week of hospital treatment and decreased authentically to the 21st day only against the traditional therapy background.

In the patients with diagnosed infected pancreatitis an extremely low chemiluminescence intensity value within the first week of hospital treatment came under notice, it not exceeding 30 mV irrespective of the patient's age and sex. The coefficient K in this group remained more than twice lower compared to the age group indexes for the entire research time. The infection process resolution criterion in the pancreatonecrosis patients has been the increase of hydroperoxide content increase in the blood serum (3, 8-fold compared to the index I max) and the increase of total anti-oxidative activity according to the chemiluminescence analysis data.

According to the contemporary idea the process of free radical oxidation is of physiological character and always attends vital processes of a healthy cell. That is why the oxidative homeostasis profound disorders detected by us in the infected pancreatonecrosis patients signalize about a massive necrosis extent, the formation of a superantigen and the overlay of bacterial contamination, which require a high flow of active oxygen forms, in the early stages of the disease already.

The chemiluminescence analysis was prospectively used by us in the complex diagnostics of infected pancreatonecrosis in 55 patients with various forms of destructive pancreatitis. Thereat, the sensibility, specificity, predictive value of both negative and positive results of the method offered by us achieved 85-90%.

There were no authentic differences of erythrocyte oxidation resistance values in sterile and infected pancreatonecrosis detected. At the admission to the hospital the maximal chemiluminescence intensity exceeded the age norm 1, 7 times, and the light-sum – 2, 1 times. The minimal erythrocyte resistance at the acute pancreatitis destructive forms occurred right after the operative intervention performance, the highest light-sum value conforming to the top of chemiluminescence intensity.

An increase of erythrocyte resistance, peroxidation and antiperoxidant defence parameters approached normal ones on the 20th day within the postoperative period in the patients with destructive pancreatitis at a favorable course of the disease.

In the 9 patients died of pancreatonecrosis a decline of erythrocyte chemiluminescence intensity was registered in the early postoperative period against the background of the light-sum double increase, that testified to the erythrocytic membranes' destabilization. There was no tendency to the increase of oxidation resistance of erythrocytes depicted in those patients in the following.

The perfection of complex diagnostics in the patients of the second group allowed minimizing the number of early traumatic surgery interferences owing to the peritonitis unascertained source cases number reduction and infected pancreatonecrosis overdiagnosis.

When defining the infected pancreatonecrosis criteria the intensive care volume in the preoperative period was extended. After the necrosis presumptive extent estimation with the help of V.B Krasnogorov's prognostic scale at the score less than 6 – mini-approach operations were performed, more and equal to 6 – supramedian and laparotomic approach operations with pancreas

abdominization, duct-rinsing drainage, peritoneal omental sac marsupialization and nasointestinal drainage.

The infected pancreatitis diagnostics improvement allowed restricting the indications for extensive and traumatic single-step interferences and expanding the indications for staging surgical sanitations.

The operations on pancreatonecrosis were performed one time and in the mode of relaparotomies: “programmed” and “on-call” ones. In the first group patients at the lack of approachable criteria of the disease course prognostication and high traumatism of operations the surgical aid was tended to be restricted by a single interference, which could include all the programmed volume. In the infected pancreatitis patients of the second group the diagnostics improvement allowed restricting the indications for extensive and traumatic single-step interferences and expand the indications for staging surgical sanitations.

As a whole, the perfection of complex diagnostics allowed improving the results of acute pancreatitis patients’ treatment and reducing the level of postoperative lethality from 32, 1% to 20, 7%.

Conclusions

1. In edematous pancreatitis patients an authentic 3, 14 times increase of the maximal luminous intensity with respect to the norm is registered at the admission. The blood serum chemiluminescence breakout amplitude in sterile pancreatonecrosis patients exceeded the age norm values 7, 16 times. In infected pancreatonecrosis patients the blood serum chemiluminescence intensity 2, 5-5-fold decrease is registered within the first week at the hospital.

2. The criteria, which are indicative of the infected pancreatonecrosis development, are the values of maximal serum chemiluminescence intensity less than 30 mV, the coefficient K less than 0, 056 c.u. with the sensibility and specificity of 92, 5% and 83, 7% accordingly. The poor prognosis criteria of the disease is the decline of erythrocyte chemiluminescence intensity against the background of double increase of light-sum and the lack of a tendency to the increase of peroxidation resistance of erythrocytes in the course of the disease.

3. The perfection of complex diagnostics and prognostication of pancreatonecrosis severe forms course allowed improving the results of acute pancreatitis patients’ treatment and reducing the level of postoperative lethality from 32, 1% to 20, 7%.

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Materials of Conference

THE EFFICIENCY PREPARATION «CONJUCTISAN A» IN A COMPLEX THERAPY OF PATIENTS WITH OPEN ANGLE GLAUCOMA

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In ophthalmology last years have began to apply preparation (retilamin, korteksin, oftalamin, semak etc.) in therapy of an atrophy of optic nerves, primary open angle glaucoma (POAG), also retinopathy [2, 3]. The combination parabulbar and intramuscular introductions peptide bioregul-ators is recognized the most effective at POAG [1]. We have been studying of clinical efficiency preparation «Conjuctisan A», which prepared on unique technology by the Nobel winner G. Blobel for the firm VitOrgan (Germany) [3, 4, 9]. Eye drops «Conjuctisan A» are widely applied in Germany for the purpose to increase functional activity of retina and an optic nerve [4, 6-10].

Research objective is researching of comparative efficiency of application «Conjuctisan A» as a magnitoforez and subtenonal introductions in complex therapy of patients POAG.

The investigated patients have been divided into 2 clinical groups comparable on age and general somatic status. Dr A.V. Svirin (2003) have offered effective operation (in Russian SIKG) - subtenonal implantation of a collagen sponge [5] for treatment glaucoma optic nerve atrophies. We develop updating of this operation: instead of soaking sponges with simple physiological solution we apply «Conjuctisan A» [3]. Operation SIKG with «Conjuctisan A» was made to 47 patients (51 eyes) POAG.

To 17 patients (34 eyes) second group with II and III stages POAG was made magnitoforez on the «Pole-2» device. Frequency of device 25 hertz, pulsing exposition - 10 minutes, round inducers, a direction of a magnetic field "North-south". Preliminary to patients was entered «Conjuctisan A» podconjuctive on 0, 25 ml into both eyes. In total there was done 5 procedures 2 times a week. Middle age of people - 57, 2±3, 4. We investigated reactions of 10 men and 7 women, including 14 eyes on developed stage and 20 eyes on far come.

As a result of treatment we found out: preparation «Conjuctisan A» provides authentic increase of visual acuity and decrease IOP in both groups of patients. After operation visual acuity has raised with 0, 48±0, 03 to 0, 56±0, 02 in 1 month; after a course physiotherapy treatment - with 0, 43±0, 03 to 0, 51±0, 02. In the same terms after operation level IOP has gone down with 26, 4±1, 3 to 26, 4±1, 3 mm Hg, and after magnitoforez - with 23, 2±1, 3 to 18, 5±1, 2 mm Hg. Directly as a result after magnitoforez visual acuity increase on 55, 9 % of eyes and decrease in level IOP on 67, 6 % of eyes is fixed. Probably, fall IOP at patients POUG is caused by specific normalising influence preparation «Conjuctisan A» on cortex departments of the visual analyzer. Improvement of linear speed of a blood-groove in an orbital artery is direct after magnitoforez has on the average made 1, 1-1, 2 times.

In conclusion: Comparative researches of efficiency of application peptide regulator «Conjuctisan A» as a method of subtenonal and magnitoforez have shown, that on dynamics of visual acuity and decrease in level of intraocular pressure, microcirculation improvement conservative application of a preparation does not concede operation subtenonal implantation of a collagen sponge,

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Short Report

INFLUENCE OF THIAMIN PREPARATION ON EXPERIMENTAL MYOCARDIAL INFARCTION

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Brief

The purpose of the work was to develop a new approach to myocardial infarction treatment using the preparation of thiamin group elaborated by the Research and Develop Institute of biochemical synthesis of the RAS Ural Branch on the basis of acute myocardial infarction experimental model.

After the MI experimental model development the simulation of the process was performed on 30 intact nondescript male white rats. Two groups of 15 animals were formed: the main group of animals given the preparation "117" intraperitoneally in the dosage of 40 mg/kg daily, and the control one formed of the animals, which intraperitoneally were introduced the normal saline solution of sodium chloride. Taking the animals out of the experiment was carried out on the 1st, 5th and 7th day. Besides visual estimation, the cardiac muscle was examined photo-optically in the left ventrical necrotic zone, near-infarction zone and the zone remote from the lesion.

The research results testified that the administration of the compound "117" forms a more favourable morphofunctional picture in the experimental infarction animals' myocardium in 1-5 days already due to the expansion in the number of hypretrophic muscles located in the circumferential direction from the necrosis of regions; an intensive fibroplastic reaction and vessels' new formation are registered as well.

In spite of the acute MI and postinfarction lethality development rate gradual decline, the myocardial infarction still remains the principal cause of lethality and morbidity [1-6]. The AMI patients have a high risk of the subsequent cardiac malfunctions, the cardiac arrest emergency, cardiac angina, cardiac failure, cerebral crisis, repeated infarction among them [7]; about one third of the patients die throughout a year after the AMI (mainly because of the cardiac arrest emergency), that makes this disease the death rate leading cause [8]. In the Recommendations of the working group of the European Society of Cardiology (2006-2008) and in the National Recommendations based upon the first ones the treatment of ACD (MI among them) is based on the application of thrombin inhibitors (heparin) and antithrombocytic agents (aspirin, thienopyridines, glycoprotein thrombocytic IIb/IIIa receptors' blockers), which can be combined with beta-blockers, nitrates and calcium antagonists if needed [9-11].

To some extent all these requirements are met by the "117 compound" from the thiamin group ("117 compounds"), elaborated by the Research and Develop Institute of biochemical synthesis of the RAS Ural Branch and possessing anticoagulant and disaggregant properties [12].

In connection with this the purpose of the present research has become the study of the influence of the preparation 117 on the experimental myocardial infarction development.

Materials, methods of myocardial infarction research in the experiment on white nondescript rats

Methods of research

After the MI experimental model development the simulation of the process was performed on 30 intact nondescript male white rats. The preoperative anaesthesia was carried out by means of ether-air mixture inhalation. The surgical field was shaven off and treated with the preparation "Ecobreeze". There was no intraoperative lethality registered in the course of myocardial infarction model creating. Taking the animals out of the experiment was carried out by means of decapitation after their preliminary being dropped-off to a narcotic sleep state.

There were two groups of 15 animals formed from the animals with the myocardial infarction experimental model: the main group – made of white rats with average body weight of 248±10 g, which daily were intraperitoneally introduced the preparation "117" (without anaesthesia) in the dosage of 40 mg/kg; and the control one – made of the animals with the average body weight of 241±12 g, which were intraperitoneally introduced the normal saline solution of sodium chloride.

Taking the animals out of the experiment was performed on the 1st, 5th and 7th day. The organ recuperation for the following histo-morphological investigation was carried out with the fixation of the material in formalin.

Besides visual estimation, the cardiac muscle was examined photo-optically in the left ventrical necrotic zone, near-infarction zone and the zone remote from the lesion. The material taken for the photo-optical microscopy and morphometry was fixed in neutral formalin, the myocardium tissue microslides were colored by hematoxylin-eosin.

Research results

The acceptability of the "117 compound" by the animals was evaluated as rather satisfactory one: there were no pain reactions and necrobiotic changes in the injection site, operative wound purulence and empyema detected in any case; and only in 20-30 minutes after the injection of the preparation there was a retardation of animals with the sound-and-light irritant reaction inhibition registered, which lasted 40-45 minutes; then there were no behavior differences with

the untreated animals detected. There were no respiratory failure, nutritional liquid intake disturbance registered, as well.

On the first day after the surgery without the preparation administration the infarction zone localized in the left ventricle wall (transmurally in the majority of the cases) was represented by cardiac myocytes with karyolysis, plasmolysis and plasmorrhexis phenomena. A moderate diffuse infiltration by segmental leukocytes without forming a demarcation zone was registered. In the adjacent structures there occurred oedemata, endomysium vessels' repletion phenomena with the formation of sludge-complexes. On the first day of the myocardial infarction with the administration the necrotic zone also localized in the left ventricle wall (subepicardially in most cases) was represented by cardiac myocytes with karyolysis, plasmolysis and plasmorrhexis phenomena. The demarcation zone had not been forming yet. In the infiltrate there appeared lymphocytes (immune-competent cells) in small amounts. The necrotic zone infiltration is minimal.

On the fifth day of the myocardial infarction without the preparation administration the infarction zone was determined as mainly transmural. The necrotized cardiac myocytes were surrounded by a demarcation bank; the granulation tissue formation signs were detected; fibroblasts and hemo-capillary tubes appeared. In the adjacent structures there was detected a spread of the infiltrate through the endomysium. In the same period of the myocardial infarction with the administration the lesion zone was displaced with the granulation tissue represented by fibroblasts, fine collagen fibers and multiple sinusoidal capillaries. The granulation tissue was infiltrated by lymphocytes, macrophages. Polymorphonuclear leukocytes were singular.

On the seventh day of the myocardial infarction without the preparation administration the infarction zone in the left ventricle wall was characterized as a transmural one in 100% of the cases. Histologic signs of the organization stage (the formation of granulation tissue round the necrotic zone with a great amount of fibroblast and macrophages, sinusoidal hemo-capillaries substituting the affected area) at the preserved disintegration of the muscle cells and preserved infiltration of the myocardium by lymphocytes and segmental leukocytes. In some cases a marginal position of leukocytes with leukopedesis signs.

On the seventh day of the myocardial infarction with the administration the necrotic zone was fully substituted by granulation tissue, wherein numerous sinusoidal type hemo-capillaries, fine collagen fibers being formed, intercellular substance, a significant amount of functionally active fibroblasts and macrophages were detected. The cellular structure of the infiltrate is lymphocytic with a small amount of polymorphonuclear leukocytes. In the adjacent areas of the myocardium the signs of interstitial edema retained, the endomysium vessels were belled and sanguine.

Discussing

A principal feature of the results got at the 117 preparation application at the experimental myocardial infarction has become the leukocytic reaction inhibition in response to the arising inflammation, that has lead to the restriction of the necrotic zone and earlier emergence of reparative processes. It is interesting that the obtained data align principally with B.G. Yushkov's (1974) findings testified that myocardial infarction in the patients with a higher leukocytosis proceeds more severely, than that in the patients with leuko-inhibitory properties of blood serum. Taking into account the fact that at the development of myocardial infarction there appears a systemic and local inflammatory response [13-15], it seems possible to picture the main mechanism of the 117 preparation action as an anti-inflammatory one due to the change of the fourth phase of inflammation according to A.M. Chernukh [16] from the leukocytic type into lymphocytic one.

Conclusions

1. The preparation 117 influences the experimental myocardial infarction course in white non-pedigree rats effectively, restricting the necrotic zone and causing earlier development of reparative processes.

2. The main curative effect of the preparation 117 at the experimental myocardial infarction is conditioned by its anti-inflammatory action.

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ROLE OF COLLECTIVE IN PERSONAL SELF-EVOLUTION

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Among the variety of organizational-pedagogical problems, which have to be solved at modern school, the class collective organization problem is a top-ranked one. The teacher should be involved into the mutual relationship in a children's collective, organize professional intercourse with the pupils, cultivating humanity-oriented values. Self-development can be considered as an active qualitative transformation of a child's inner world promoting his original creative self-realization. The acting force of this self-development can be an ambition to unlock one's creativity, search for new opportunities for self-realization, and comprehend one's possible talents.

The pedagogue should be involved into the mutual relationship in a children's collective, organize professional intercourse with the pupils, cultivating humanity-oriented values, helping a personality in his self-development using the possibilities of the children's collective.

The participation of Russia in the Bologna Process demands further democratization of the system of education that is directly connected with the upbringing perfection and its strategy determination. The integration into the world's educational space sets lots of problems before our society. In particular, let us note that the idea of "upbringing" itself is mainly indicative of the native pedagogy and practice. If we want to keep our originality, it is necessary to understand (and act in accordance with this understanding) how important and worthful is to preserve Russian traditions and accumulated experience of higher school in the formation of the student's personality evolution, in particular [2, p. 44].

The teacher's activity should be clearly planned, in the center of his work there should be the personality of a child and favourable conditions for its becoming and self-development. The personal-professional self-development will help the teacher therein. This self-development can be considered as an active qualitative transformation of his inner world promoting his original creative self-realization in the profession by himself. Only a pronounced ability of the teacher to active transformation of intrinsic and extrinsic motives of his activity affords an opportunity to read them as a prerequisite to the personal and professional self-development. The acting force of this self-development can be an ambition to unlock one's creativity, search for new opportunities for self-realization, and comprehend one's possible talents [3, 66].

The evolution of a personality is also exercised in a collective, that is why the pedagogical problem of the primary school-aged children collective development needs for continuative attention. It should be born in mind that without the collective's self-management the real personality development in it is impossible. Therefore, we consider the role of a collective in the process of self-management as an example.

The pupils' self-management – is a form of learners' collective life activity organization providing the development of their independency in making decisions and decisions' realization for the achievement of socially meaningful objectives [4, 206].

Among the variety of organizational-pedagogical problems, which have to be solved at modern school, the class collective organization problem is a top-ranked one. The teacher should be involved into the mutual relationship in a children's collective, organize professional intercourse with the pupils, cultivating humanity-oriented values. Approval or condemnation, support or rejection of any view points by the collective form a public opinion, which is not only a collective's characteristic, but is also used as one of the methods of pedagogical interaction. The public opinion method consists in the attraction of educatees to the development and specifying socially and morally valuable requirements to each other, setting and realiza-

tion of socially and personally meaningful prospects, exercises a dominant influence on the encouragement and punishment efficiency. The public opinion method purpose consists in the promotion of everything positive in the collective's life and negative developments and tendencies negotiation. However, selfhood, personalism and irresponsibility manifestations are still seen in school children in practice. It is not infrequent that junior school learners share school accessories with each other unwillingly, are ill-disposed to their equals in age, show their obduracy, indifference to those, who miss lessons because of illness, are not gratified by their mates successes [6, 4].

Effective conditions for the psychological climate creation in a pupils' collective are good relations between the group members. The problem of the pupils' collective formation is topical nowadays and demands to be studied deeply and seriously. A purposeful organization of the psychological climate in a pupils' collective consists in changing the character of official and non-official structures interconnection at various stages of the collective's development. The interaction of official and non-official systems of school children interrelations at various stages of the class collective's development is very important. Without knowing the informal system of the group interaction the teacher cannot manage the collective's development. When analyzing the psychological climate of a pupils' collective it is necessary to know: what interrelations between the groupings are; if there are groupings poisoning their minds against pedagogical requirements in the class; what the officially working core group's members represent; if the core group is a real one, i.e. determining norms; what the position of every child in the collective is.

The teacher should take all these aspects into account in his work with pupils' collectives, as every one of them is important enough to develop a positive psychological climate. On the opinion of the pedagogue Anikeyeva N.P., all groups take their special place in a collective on two hierarchies: 1. The hierarchy of groups according to authoritativeness. The reputable groups define collective ones; 2. The hierarchy of groupings according to their values and interests [1, 204].

The teacher's task – is to achieve the coincidence of these kinds of hierarchy, so that the groupings with the highest values became the most authoritative in the group.

At every stage of a collective's development it is necessary to see not only who the requirements are specified by; but also how the attitude of the children to the activity is being changed; which role the self-management in the collective plays; which changes are taking place in the activities and behavior motives of every member of the children's collective; which corrections are possible to be made, depending on the junior school teacher's professional knowledge and skills.

At the first stage the teacher deals with a formal union of children. In his classification A.N. Lutoshkin compared such a collective to a sand deposit. Indeed, like sand grains in a handful, the children are united by nothing. The teacher should take the organizational function upon himself, specify the requirements, set the rules and norms of the relationships, and – the name of the game – kindle the children's interest in modern activities [5, 73].

The second stage is defined by the fact that the core group takes part of the organizational functions upon itself. It is like a "twinkling lighthouse", and the teacher, like the light-keeper, should take care of it, i.e. take the organizational, communicative and correctional functions upon himself.

At the third stage a harmonic combination of submission and leadership, all members of a collective show mutual insistence on high standards, interest in teamwork, live out the successes and failures of the collective. Both adults and children are contributors to a common deal. There appears a real protection of a personality in the collective; conditions for personal self-

realization are created. The collective successfully carries out its activity. It is a "scarlet sail", which symbolizes a dream that came true and a sense of joy. In an analogous classification there is one more metaphor: such a collective is a "burning torch", as it becomes an example for others.

The process of development of a collective is very complicated, and in real life it is most often impossible to see clear bounds between the stages of its development.

A children's collective is the most important factor of purposeful socialization, personality upbringing. Its influence on a personality depends largely on how seriously the purposes and intents of the collective are realized by its members and understood by them as their personal ones.

Collectivity is a sense of sympathy with the group, understanding of oneself as its part, readiness to act to the good of the group and society. The upbringing of collectivity in a school collective is achieved in a variety of ways and by various means: the organization of collaboration and mutual aid in studies, labour, extracurricular activities; joint participation of school children in cultural and sport events; setting perspectives (activities objectives) before learners and joint participation in their implementation; children's and teenagers' voluntary societies' work activation.

Realizing that the teamwork organization most important method is self-management, we defined the kinds of activity according to children's missions: the participation of children in planning, development, carrying out and analysis of crucial actions of the collective; implementation of collective, group and individual missions; creative duties in the class, organization of creative breaks. That is why there were 6 groups formed for the realization of the purposes. Every pupil was in one or another group (3-4 persons in every one).

The backbone of teaching self-management of the class in our investigation was the voyage-game "Merry Train" representing a complex program of junior school children's activity organization and promoting the development of every one of them. The pupils set forth their travels in dillies. The passengers chose and had been implementing one of the 6 alternating missions for a month.

Every group of children received its name: scouts, amusements organizers, youth correspondents, letter carriers, wiser heads and lifeguards. The pieces of advice – hints stated in specially developed check lists for the junior school children – helped the travelers to fulfil their missions actively, creatively and in good faith.

Afterwards we started watching how the children behave in various situations and whether they gather in groups after their hours. The watching plan included registering the interaction between the children: how they settle among themselves; how often they quarrel; how they carry out their common deals; whether they help each other, why and where in; whether they are organized or not. How the children behaved fulfilling their traditional missions in groups and how they proved themselves during the intercourse hour when they reported on the charged affairs was taken into consideration.

On the trip the passengers of the "Merry train" took part in various competitions of cognitive and creative character, fulfilled collectively of several offered assignments (it was given in a colorfully painted ticket for every dilly). After monthly being on the way the train makes a stop destined for the analysis and summarizing the work of the whole team of every dilly and every passenger. "Where we succeeded? Where we failed? What should we take into account and make in the future?" – these questions were to be answered individually and collectively. Who was the best was decided by the whole class. During the stop a change of collective missions took place in the passenger body. The course and results of the voyage-game reflected in the class hour. The use and importance of efforts of every child and the class as a whole became apparent at the made train model inspection. The walls of the dil-

lies were decorated with pockets for assignments, and windows – with the pockets for passengers' photos. In the "Mood Screen" near the surnames of the pupils the tickets of the fulfilled assignments were placed. The travel participants collected 7 tickets got an opportunity to canvass a picture the "Mode of Transport". The most active pupils were awarded with the medals "The best scout", "The best amusements organizer", "The best youth correspondent", "The best letter carrier", "The best wiser head" and "The best lifeguard" at the year-end.

At the end of every month the children narrated about their impressions, about what they succeeded and failed in. Thus, the educational measures carried out by us allowed evoking the wish to act in a body, collectively in the children. Every member of the collective differed with a high personal responsibility for the joint activity result.

By the end of our investigation we had noticed that the children in the groups started enjoying the companionship of each other and communicate with each other. They learned how to settle and make arrangements with each other; quarreled much more seldom; started carrying out common missions hand in hand; became able to see, who needed a help; helped each other. Disagreements started taking place much more seldom, a common opinion on the problem being discussed formed quickly during the discussion. Therefore we can speak about the teacher's self-development in the process of application of educational measures, which improve the development of a collective by means of pupils' self-management. The results comparison showed that the level of junior school children collective development in the experimental class grew generally, and in the control class this growing was insignificant. For a sound growing of this level a further work over the development of the collective is required.

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EXPERIMENTAL VALIDATION OF POLYHYDROXYALKANOATES BASED BIODEGRADABLE SUTURE MATERIAL USE

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The availability of monofilaments made by 3- hydroxybutyric acid polymer melt extrusion (polyhydroxybutirate, PHB) in surgery has been investigated. The applicability of PHB suture filaments for sealing muscle-fascial wounds, one-row enteroenteroanastomosis applying has been proved. At the formation of one-row enteroenteroanastomosis there were no PHB retention sutures detected in the specimens after 100 days of observation, all the anastomoses being well-fixed. There were no complications in the form of early or delayed malfunctions, anastomosites, bowel obstruction or adhesion registered in the abdominal cavity. When studying the anastomosis zone histologic specimens after 100 days of observation a developing granulation tissue was found out.

Key words: (polyhydroxybutirate, PHB, suture filaments, muscle-fascial and intestinal sutures, one-row enteroenteroanastomosis, tissue reaction, resorbable suture material.

Introduction

The penetration of a surgical needle and filament through tissues causes damage and cell death. The presence of a foreign body (filament) promotes the macrophage excess accumulation in the inflammatory tissue, and this feature retains not less than 3-5 days. During this time no morphological features of reaction to separate synthetic suture materials are practically noticeable. The specificity of reaction to various kinds of suture materials starts manifesting itself in 10-15 days only. The inflammation degree and character dependency on the applied suture material kind in the surrounding tissues is mentioned by many authors.

The invalidity of intestinal anastomoses – is one of the most frequent causes of early postoperative complications and lethality in surgical gastroenterology. The given complication occurs in 1, 5-3% of stomach and duodenum operations, in 2, 8-8, 7% of small and in 4-32% - large bowel operations. That is why the creation of optimal conditions for suture and gastrointestinal tract anastomoses healing – is the principal reserve of improving the nearest results in the patients operated on their stomach and intestinal tract.

Thus, when applying an intestinal suture, the defining moments are technical features of fistulization and characteristics of the suture material, which should cause the minimal tissue reaction of the intestinal wall.

Materials and methods

The monofilaments are made of the highly purified 3-hydroxybutyric acid polymer (polyhydroxybutirate, PHB) samples synthesized on the technology of the Institute of biophysics of RAS. The filaments are obtained by means of the PHB melt extrusion, using a laboratorial autonomic extrusion machine Brabender® 19/25 D (Germany). The physical and mechanical properties of the filaments are defined in a universal electromechanical tensile-testing machine Instron 1122 (Great Britain) with the extension rate of 100 mm/min. The filaments had the diameter of 0, 15-0, 17 mm (metric dimension 2), the absolute strength of 300 MPa, the elasticity modulus of 3GPa and a high mechanical strength in conditions of static and cyclic stressing (up to 100 MPa). The filaments are used for sealing muscle-fascial wounds and one-row enteroenteroanastomosis applying. The animal experiments are performed by the authority and in accordance with the Research Programme approved by

the Committee of the Institute of Biophysics of RAS on Bio-Ethics and Ethical Committee of KrasSMA named after Pr. V.F. Voino-Yasenetsky. The experimental animals (Vistar-line rats raised in the nursery of the Institute of Cell Biology and Genetics of RAS) were given inhalation anaesthesia and a 2 cm long vertical section of skin and muscle was performed on the right huckle in aseptic conditions; three PHB sutures (total length of 3, 0-3, 5 cm) were applied to the muscle; the skin was sealed with silk. In the group of comparison (control) a surgical gut, metric dimension 2, "Catgut 0, 41101" trademark (HELM PHARMACEUTICALS GMBH, Germany), was used. The possibility to use PHB filaments to apply an intestinal suture was tested on both sex non-pedigree dogs weighing from 12 to 20 kg. The animals were divided into 2 groups. The first group or the group of comparison included 8 animals, which an "end-to-end" enteroanastomosis with the help of a one-row serous-muscular-submucosal U-bend suture was performed on. As a suture material a wide-spread Vicril 3.0 with an atraumatic needle was used. The second group under research consisted of 9 animals, which an analogous anastomosis with the help of PHB filaments was performed on.

The study of total tissue reaction to PHB filament was carried out by histological methods. To that effect the tissue fragments in the locus of filament implantation were taken; the material was fixed in 10%-formaline and put into wax; 5-10 cm thick sections were made of the blocks and were analyzed, using Image Analysis System "Carl Zeis" (Germany); the intensity and duration of the inflammation, the fibrous capsule formation dynamics round the filament and its cellular composition were evaluated. The activity of cellular elements was judged on their average quantity per high power field at the analysis of 15 visual fields. The definition of fibrous capsule (FC) thickness and fibroblast rowness (FR) in it was carried out on the morphometric method of V.P. Yatsenko (Yatsenko and co-authors, 1986).

Results and discussing

The PHB filaments, as analogous to catgut, safely held the muscle-fascial section wound edges together for the entire postoperative period. The wound repair in all the experimental animals occurred by primary intention. The microscopic state in the PHB filaments implantation site on the 7^{th} day after the operation was characterized by an insignificant tissue edema and single fine necrotic zones round the implanted filaments. The filaments were mainly surrounded by macrophages and lymphocytes, also neutrofils and fibroblasts. In 2 weeks the inflammation sings diminished, an insignificant tissue puffiness round all the implants being preserved; leukocytic cells still occurring in the inflammation zone; the beginning of fibrous capsules formation round the implants being registered. The tissue reaction round the PHB filaments concerning the inflammatory force was considerably less manifested compared to the reaction to catgut. In 4 weeks after the operation the thickness of fibrous capsules round the PHB filaments made 172, 23±13, 64 um, that was much less than that in the catgut implantation site. The number of active macrophages with a great amount of excrescences and cellular lysosomal structures (up to 11-12 per high power field) kept on growing. The capsules were represented by fibroblasts and collagen fibers, which started forming into batches. In 8 weeks the microscopic state of tissues in the experimental and control filaments implantation zone remained practically without changes, as well as the capsules' thickness and their cellular composition did. In the zone surrounding the filaments a great number of active macrophages was still registered. The FC thickness achieved 514.21+12.01 um round catgut in spite of its destruction features in this very term. The collagen fiber batches in the FC round catgut were much thicker and took practically the capsule's total volume. 16 weeks after the implantation a significant thinning of the capsules round the PHB filaments was registered, their average thickness being reduced up to 54, 09±3, 28 with the fi-

broblast rowness (FR) at the level of 4, 64±0, 37; the number of active macrophages in the tissues being adjacent to the implant still remained at the high level. The FC thickness achieved 514.21+12.01 um round catgut in spite of its destruction features in this very term. The collagen fiber batches in the FC round catgut were much thicker and took practically the capsule's total volume. In 24 weeks after the operation a further involution of the fibrous capsules round the PHB, the CT reduced thereat up to 33, 73±2, 05 um accordingly. Fully formed collagen fibers prevailed in the capsules, active phagocyting macrophages still being present. In the catgut implantation site, in spite of its active destruction (by 4 months in hadn't been detected in the tissues), solid capsules remained unchanged. In 16 and 24 weeks after the implantation of catgut the CT made 342, 00±9, 68 и 272, 14±4, 11 um accordingly.

A further tissue state monitoring in the animals, which were implanted the PHB experimental filaments, testified that there were no strong changes in the implanted filaments' state taken place. 9 months after the operation there were no negative occurrences in the zone of implantation registered. The capsule's thickness round the filaments in separate animals made 20-40 um. The implants were surrounded by sound tissues of newly formed fibers, which were centered round the polymer filament. In 12 months there was practically no fibrous capsule round the implants registered. In the close proximity to the polymer filament, circumferentially and also in the adjacent tissues, a considerable amount of mono- and polynuclear macrophage cells was still registered. In this term there was no negative reaction of the tissues to a foreign body registered in spite of the polymer filament presence in the animals' muscle tissue.

The morphological methods of research of tissues in the zone of intestinal anastomosis included a macroscopic description and histologic characteristic of preparations. Macroscopcally (according to the data of autopsy) the effusion presence, adhesive process intensity in the free abdominal space, appearance of enteroenteroanastomosis, its patency, cicatrical changes presence in the zone of intestinal sutures application were evaluated in 100 days.

At the autopsy all the anastomoses were patent and well-fixed, there were no signs of local and extended peritonitis registered in any of the animals. In all the first group animals there was a moderate adhesive process involving the omentum and mesostenium with the presence of solid sagittal commissures detected in the anastomosis area. In two animals there was a moderately expressed cicatrical deformation registered in the anastomosis application area. Vycril sutures were clearly visualized.

In the animals of the second group the adhesive process was considerably less manifested. Macroscopically in the area of anastomoses there was an insignificant thickening of the intestinal wall registered, there was no cicatricial deformation in the intestinal suture performance area fond out, the PHB filaments were not visualized.

Similar results were got at the analysis of morphological preparations of anastomoses zones in the animals of both groups. At the anastomosis level a developing granulation tissue represented by the vessels of capillary type, fibroblasts, epithelial, plasmatic cells, lymphocytes, eosinophils and single leukocytes were defined. There was no intestinal walls' layers deviation detected.

Thus, the results of experimental studies of PHB filaments for the performance of a manual serous-muscular-submucosal U-bend intestinal suture found out the lack of peritonitis and anastomosis malfunction signs, insignificantly expressed formation of commissures in the intervention area, lack of inflammatory response of the intestinal wall to the filament. It allows taking a favourable view of the PHB filaments application preliminary results for the intestinal suture formation and requires further studies.

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COMPETITION DEVELOPMENT AT REGIONAL FOODSTAFFS MARKET

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The Sverdlovsk region is the fifth largest region in Russia and the largest region in the Urals situated on the border between Europe and Asia. At present competitive relations in agricultural and provisions complex are not developed enough and do not correspond to developed market. In this case it is necessary to develop the theoretical framework of effective modals of competitions and its peculiarities during contemporary stage of market development.
The programme implies the development of healthy competition on provisions market, agricultural producer's support, permanent monitoring of prices on agricultural raw materials and food supply, and also realization of measures directed to improvement of food products trade regulation, including their security and quality requirements conditions. As a result of the programme realization, the rise in stabilization of the provisions market in the Sverdlovsk region and the increase in foodstuffs production share in gross regional product output are expected.
Key words: provisions market, competition, provisions safety, food management.

Competition as a form of economical activity organization is one of the basic institutions on provisions market, the most important condition of its effectiveness. The level of its development is the main index of market reforms. Gradual globalization of the economy, active involvement of Russia in international economical processes, need to meet the requirements of competitive market set goals of full analysis of factors, forming competitive strategies of market subjects. In developing market conditions the influence of the factor of competition between national and regional markets on strategic and investment attraction of the main producers as well as regional agricultural systems has increased significantly.

The development of the competition is one of the most important parts in institutional and structural transformations. At present competitive relations in agricultural and provisions complex are not developed enough and do not correspond to developed market. In this case it is necessary to develop the theoretical framework of effective modals of competitions and its peculiarities during contemporary stage of market development.

This programme is especially urgent for industrially-developed regions. In particular, the Sverdlovsk region is the fifth largest region in Russia and the largest region in the Urals situated on the border between Europe and Asia, its territory is about 194.3 th. square km. The population of the region is 4364 mln. people. Yekaterinburg is the capital of the region (1346.3 th. people), the fourth largest city in Russia. There are 47 towns in the Sverdlovsk region. The main economic centres (besides Yekaterinburg) are Nyzhny Tagil (377 th people), Kamensk-Uralsky (183 th), Pervouralsk (159 th), Asbest (104 th), Serov (100 th). The specific character of this territory is the predominance of the urban population over the rural population. On 01.01.2007 the urban population of the region was about 3659 thousand people and the rural population was only 740 thousand people.

The regional provisions safety (as everywhere else) depends on the development of agro-industrial complex (to a greater extend than in other territories), as well as on the development of the provisions trade.

Since the beginning of this year the Sverdlovsk region has been the fifth subject of the Russian Federation in terms of the retail trade turnover and the second one in the Urals. At the beginning of 2007 there were 19.5 thousand of retail outlets in the Sverdlovsk region. In 2007 the retail trade turnover accounted for 61.4% of small enterprises, and the share of agricultural markets was about 15.2%. The share of provisions goods in the retail trade turnover accounted for about 45%, the annual average increase in

provisions turnover has been 15.6% for the last 3 years.

In 2007 the average monthly sale per person was 7, 4 thousand rubles in the region (increase by 29.5%), this tendency is believed to remain until 2010. The consumers purchasing power is increasing as incomes are growing. In 2007 the population could buy 15.8% more foods, included in the minimum set than in 2006.

It is necessary to admit that the development of the provisions trade is closely linked to the import of commodities. Import share in the whole volume of provisions resources is more than 40%, which threatens the provisions safety of the territory.

Providing country and regions provisions safety is one of the topical objectives of the state in the field of social and economic policy. The cause of this fact is also aggressive foreign countries policy in food supply sector.

The programme implies the development of healthy competition on provisions market, agricultural producer's support, permanent monitoring of prices on agricultural raw materials and food supply, and also realization of measures directed to improvement of food products trade regulation, including their security and quality requirements conditions.

The main programme principles are:

- providing healthy competitive environment by letting access on the provisions market for companies of all types of ownership;
- "programme-goal" method of forming provisions recourses;
- producer's protection (domestic RF subject's support – the Sverdlovsk region), both big business by developing private state partnership with projects investments and small and medium-size business by infrastructure creating, assistance to associations creating through all range of life cycle of local products (brands), approximation of informational and educational programmes to the agricultural producer;
- self-developments of the territories of the bases of their diversity at the expense of their internal reserves taking into account their specialization and optimal local resources usage;
- supply and demand self-regulation due to increasing role of self-regulating non-commercial organizations in terms of providing provisions safety, independent expertise and monitoring;
- popularization of provisions that are ecologically clean and have medical and preventive effect – "prolonging life" by wide information enlightening work, educational programmes, internet resources, mass media, etc.;
- providing state support from regional budget to wholesale provisions complex organizations, domestic agricultural producers of raw materials and provisions on competitive basis;
- making managment decisions taking into account the analysis of monitoring data about forming and supporting of provisions resources;
- providing transparency of information about the state of provisions market.

The goals of the programme are:

- development of competition on the provisions market in the Sverdlovsk region aimed to strengthen the provisions safety in the region on the basis of forming stable own base of producing raw materials and provisions products, providing regular supply of qualified and safety products on the region provisions market;
- provisions market optimization due to its saturation and more complete satisfying of regional consumers demand. Creating conditions for effective functioning of consumer market in the Sverdlovsk region;
- creating conditions for business competition by means of anticompetitive actions preclusion;
- removal of extra administrative barriers on agricultural market and preclusion of unfair competition on the provisions market.

To achieve these goals it is important to solve the following problems:

- achievement of guaranteed volume of production of qualified provisions raw materials basically due to local production according to the standards;

- development of enterprises of processing, packaging and storage of output at the place of production and sale;

- improvement of the provisions market infrastructure by means of development of distribution network and modern types of trade;

- realization of antimonopoly control directed to retaining inflationary processes and prevention of market destabilization;

- protection of consumers rights to receive reliable information about the product;

- execution of legislation standards of pricing for socially important goods of bare necessity;

- revival lost directions and production technologies of some types of goods during the reforms years;

- creation and introduction of new types of foodstuffs, usage of new technologies of agricultural products processing and storage;

- development of cooperation (credit, production, supply and sale) to reduce the number of middlemen;

- strengthening specialization and concentration of agricultural enterprises;

- interconnection of the programme with other regional programmes aimed to improve the population living standards in the region.

The following measures have been worked out of the programme:

- **organizational** – directed to the creation of competition conditions development on the provision market of the region interactively with regional enterprises of agro- industrial complex, the growth of business activity by means of development of conception to support of small and medium-size business in the field of agro- industrial complex and the provisions market, the development of agricultural territories at the expense of increase of agricultural products output.

- **financial and economic** – ensure financing the projects of development, existing agro-industrial, logistical and commercial enterprises in the region at the expense of agro- industrial complex, regional budget and other sources.

- **technological** – provide the adoption of new technologies of agricultural production, foodstuffs production, storage, processing, packaging and sale of agricultural production in the region. Directed to introduction of modern technologies of transportation, storage and sale of foodstuffs and their production.

- **social** – provide health improvement, increase in life duration of the population, quality improvement of foodstuffs consumed, price factor decrease, increase in number of foodstuffs and their variety in consumer basket, forming the list of socially oriented trading organizations, stabilization of wholesale prices on main the basic socially important groups of products.

Therefore, as a result of the programme realization, the rise in stabilization of the provisions market in the Sverdlovsk region and the increase in foodstuffs production share in gross regional product output are expected.

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NEW ASPECTS OF QUALITY EVALUATION OF VEGETATIVE FOODSTUFFS

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Antioxidant activity is a new aspect of quality of vegetative foodstuffs and food raw materials. Unbalanced feed evoke economic consequences – decline of labor productivity, increase in expenses of national public health services. It is known, that about 30% of expenses of national public health services in Europe cause by the illnesses connected with worthless diet. Free radicals add much to the progress of various diseases: ischemia, glaucoma, defeats of lungs, blood diseases, arising of tumours, as so as malignant. Antioxidants are capable to reduce amount of free radicals and to protect macromolecules in living cells. The mane sources of antioxidants for human organism are vegetables, fruit and other foodstuffs made of vegetative raw materials. Organization of proper antioxidant diet allows protecting human being from free radicals.
Keywords: quality control, foodstuffs, antioxidant activity, vine, beer, fruit, vegetables, express methods.

To provide the mankind with foodstuffs according to physiological standards is still an actual problem. A feed from infancy till last days affects human organism. Food substances convert in human body and define its health, health of its posterity, and influence on the age of life. For this reasons the quality of food is one of the major factors, which define human health.

Scientific opinions on a role of food substances in metabolism have been formed in the middle of XIX century. Considerable amount of information about the significance of biological macromolecules, vitamins and inorganic ions for functioning of organism has been saved up at that time. A little bit later, in the beginning of XX century, the theory of the balanced feed was formed.

The diet of the modern person is based on knowledge about physiological norms for energy, for basic nutrients, for macro- and microelements. An unbalanced feed, both insufficient, and abundant, can cause illnesses. It is known, that excessive diet is one of the reasons of obesity and cardiovascular diseases. Lack of iodine causes not only dysfunction of a thyroid gland, but also delay of mental development, which could be avoided. Iron-deficient anemia slows down intellectual development of children and raises risk of diseases and death of pregnant women.

Unbalanced feed evoke economic consequences – decline of labor productivity, increase in expenses of national public health services. It is considered, that about 30% of expenses of national public health services in Europe cause by the illnesses connected with worthless diet [1].

Now it is known, that free radicals add much to the progress of various diseases: ischemia, glaucoma, defeats of lungs, blood diseases, arising of tumours, as so as malignant [2]. Abundance of free radicals in human organism formed due to various reasons. There are adverse ecology, xenobiotics, taken with food, smoking, and even psychological stress.

The substances, capable to reduce amount of free radicals and to protect macromolecules in cells, named antioxidants (AO). The mane source of antioxidants for human organism are vegetables, fruit and other foodstuff made of vegetative raw materials or specially created biologically active additives. The urgency of the above-listed reasons has led to high necessity of an evaluation of integrated antioxidant properties of these products. It's clear, that organization of proper antioxidant diet demand the elaboration of simple and cheap methods for the analysis of integrated antioxidant properties of products.

In Ural state university of economics the new method of research integrated antioxidant activity has been developed [3]. With the use of this method the broad audience of vegetative foodstuffs has been analyzed [4]. Results of this research leaded to conclusion, that the parameter of antioxidant activity

(AOA) can be used for quality evaluation of food.

Fruit and vegetables contain a considerable amount of substances, which provide AOA. In figure 1 results of AOA measurement of industrial and fresh juices of vegetables and fruit are presented.

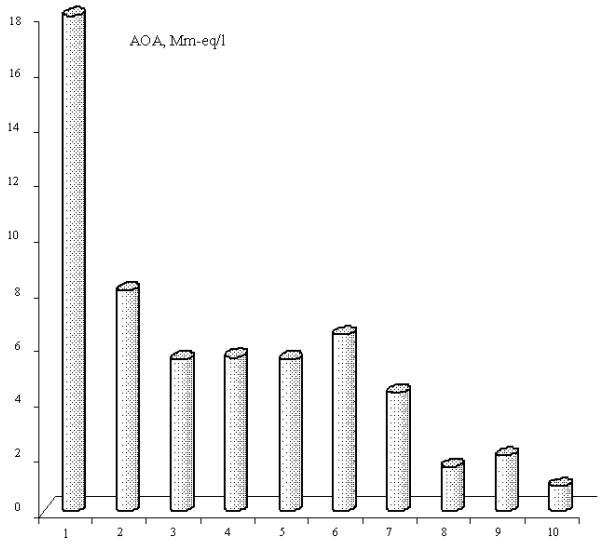

Fig. 1. AOA of fruit and vegetable juices*

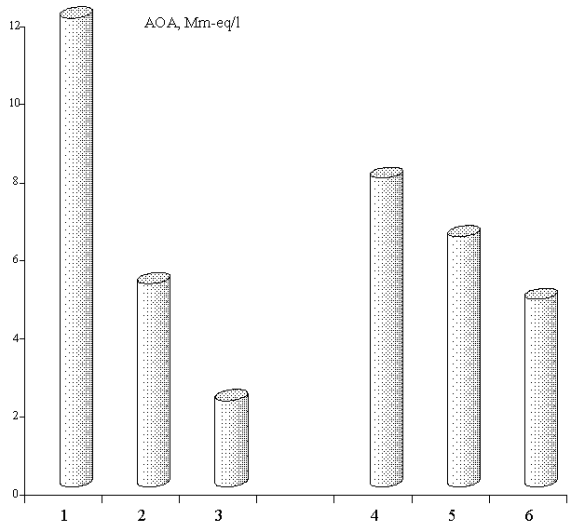

Fig. 2. AOA of tea**

***** Fresh juices: 1 – black currant, 3 – Nefhelum lappaceum, 4 – kohlrabi, 5 – sweet pepper, 6 – oranges. Juices of industrial manufacturing: 2 – black currant; 7, 8 – orange; 9, 10 – tomato.
** Black tea – 1, 2, 3. Green tea – 4, 5, 6. Tea bags – 3, 6.

The highest values AOA have been found in fresh juices of a black currant, Nefhelum lappaceum, oranges, kohlrabi and pepper sweet. AOA of fresh juices was a little bit higher, than of industrial ones. AOA of industrial juices of different manufacturers could differ twice. That fact is possible due to different quality of initial raw material.

In figure 2 AOA of various kinds of tea are presented. In some samples of black tea this parameter was nearly twice higher, than in green tea. Higher level of AOA can be caused by high quality of raw material, proper processing that allow to preserve tea antioxidants. It is necessary to note, that AOA of black tea bags was significantly less, than those of leaves tea and green tea bags.

In table 1 the results of wine and beer investigation are shown. AOA of those beverages connected with technology of their manufacture. AOA of wine and beer correlated with quantity and quality of the vegetative raw materials used for its manufacturing.

Nonalcoholic beer has a least AOA. The highest AOA was found in dark beer with 15-16% extractive substances in a mash. It is necessary to note, that AOA in the same kinds of beer from different manufacturers could differ nearly twice.

The general level of polyphenols in wine depends on a sort of grapes and a way of drink manufacturing. Skins of grape berry contain 9-10 % of polyphenols, pulp – 85-90 %, and seeds – 2-6 % of weight of a berry. This fact is very important because white and red wine has different contact time of skins and seeds with juice. Different ways of winemaking lead to a different value of AOA in red and white wine.

Wine is falsified often. In figures 2 and 3 AOA of 60 samples of white and red grape wine are presented.

Table 1. AOA of beer and wine

Group of beverages		AOA, Mm-eq/l
Beer	nonalcoholic	0, 4
	12% extractive substances in a mash	1, 4 – 0, 8
	15-16% extractive substances in a mash	2, 0 – 2, 2
Wine*	Red	17, 4
	Pink	11, 0
	Port wine	9, 6
	Wight	5, 4

*Average AOA for group (not less than 10 samples).

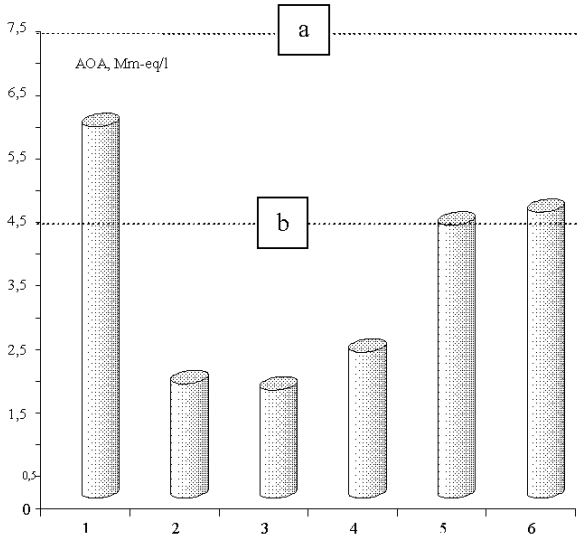

Fig. 3. AOA of wight wine*

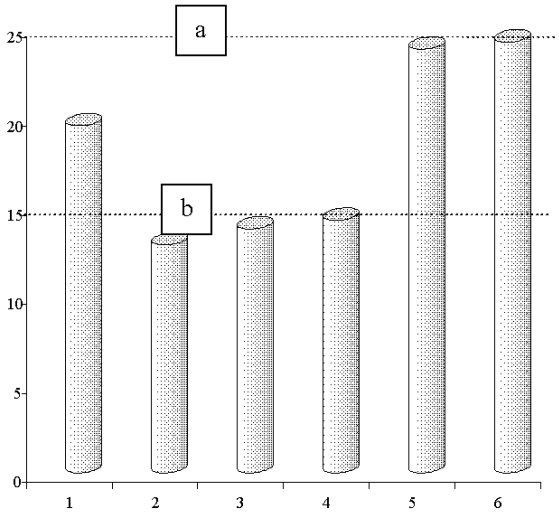

Fig. 4. AOA of red wine*

*1 – average level fore group, a – higher level, b – lower level; 2, 3, 4 – diluted samples; 5, 6 – proper wine.

At the same time these samples have been investigated by the method of capillary electrophoresis (CE), for identification natural and forged wine. AOA of samples of the wine identified by CE as diluted, was much lower, then AOA of natural wine.

Thus, the information about AOA of vegetative foodstuff has a significant importance. Antioxidant activity is a new sign of quality of vegetative foodstuffs and food raw materials.

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Materials of Conferences

ANALYSIS OF ASSESSMENT OF REAL ESTATE ON NEURAL NETWORK

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The goal of the development is a making the site ”Assessment of real estate on neural network” for granting user possibility of the study of the procedures of the assessment of real estate and analysis of the assessment of real estate on neural network. This site gives a user a possibility of study of the procedures of the assessment of real estate: spent method, a revenue method, a method of the benchmark analysis of the sale. Also undertaking the analysis of the assessment with use trained neural network.

The core of this paper is analysis of assessment of real estate in Volgograd at the end of year 2006. This analysis based on artificial neural nets modeling. We was investigated predictive index of real estate requirements. Estimation was carried out using Deductor (neural modeling tool). Effective model of neural nets for forecasting problem solving is multi-layer perceptron. During learning neural net with back-propagation algorithm, neural net is capable to made most probable forecast if learning sample is well exact and wide. Base for learning sample was created from data of Federal Service of Staticstics from 1995 till 2004. As an input information were used following activities: average coefficient of flats’ price increasing (%); average price of rent of holding (RUB per 100 square meters); average costs for forming housing (thousands RUB per square meter); commission of blocks of flats (million square meters per year). As in output information was used index of blocks of flats need per year. As units of blocks of flats need we take minimal space of housing (12 square meters). Macros BG_ExportToDeductor.xla allowed to export data to Neural Analyzer 3.0 (one of Deductor’s modules). There are statistical sampling data are tuned in this window. Field 1 is informational because it contain information about years of statistical examina-tion. There are net parameters settings in this window: algorithm choice, function choice, steepness choice, and so on. In this case back-propagation algorithm was choose. It is necessary to make up learning sample for experiment. In this window statistical data are inputed for operative experiment with learned neural net. Neural net is consider learned if results of experiment agree closely with testing samples. If it isn’t true then it is necessary to re-learn neural net.

Misprediction is from 4.29% till 10.34%. There are following data receiving from analysis second half year 2006. Average price of rent of holding 261%; average costs for forming housing (thousands RUB.) – 15180; commission of blocks of flats (million square meters per year) – 39; coefficient of price changing 119, 8 %. Judge by neural net’s forecast, commission of blocks of flats will be 4598. As neural net was mistaked, a result will from 4001 till 4598.

The work is submitted to the International scientific conference "Modern science technology", Tenerife, Spain, November, 20-27, 2008, came to the editorial office on 01.06.2008.

DIRECTIONS OF ORGANIZATION ACTIVITY ASSESSMENT WITH ACCOUNT OF ITS INTEGRATION AND INNOVATION ACTIVITY

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Generally, the management of any organization consists insetting and achieving its final objectives (the result) by means of creating and redistributing of the resources – financial, personnel, informative and material-and-technical. In the extended comprehension, everything that can be used by the administration of an organization for the objectives achievement, including the business processes, the configuration of which represents a concrete means of the final value accumulation for the key influence groups (clients, first of all), comprises the category of organizational “resources”. However, marking business processes out of the “generalized resources” of an organization appears well-grounded for receiving a clearer picture of the going on in the bond “resources-processes”, especially when studying the directions of the multi-industry integrated structure (MIS) participants’ interaction. For providing an analytical support for the organizational result achievement it seems well-grounded to divide this process logically into four interconnected aspects (objects of managerial influences application objects) – *Finance, Resources, Business-Processes, Products.* The state of every following aspect in this chain is the sequence of a certain state of the previous one, and so is, in a certain manner, connected with the state of every of the aspects. Every aspect is characterized by its potential, i.e. the state for a certain moment, and the activity in realization of this potential on the part of the managing subject for a certain period. The required growth of potentials cannot be realized inertially, as a matter-of-course. This growth (representing the organization development) takes place only owing to the *purposeful activities on* the previous aspect’s *potential realization.*

Thus, the very growth of the system of potentials through the assistance to their realization should be considered as one of the most important tasks of the managerial function of an organization at all the levels, and especially at the highest one – at the level

of the persons making strategic decisions, for the provision of the final objectives achievement.

The analyzed, compared to other profiled competitive structures, state of an organization potential on the aspect "Products" for the reference period beginning, and also its desired state for the beginning of the following period, forms requirements and, at the same time, detects the restrictions on all the rest potentials of the aspects in their chain. It, in its turn, makes an opportunity to come reasonably to the determination of possible directions of the integration of an organization with other structures, the directions requiring the realization in the reference (in case of strategic partnership) and following periods.

But the reflection itself, recording and impact evaluation of integration efforts of an organization, at the efficiency and effectiveness of its work is exercised by means of separation of that art of the aspects' potentials for the beginning of the reference period and their implementation during this period, the potentials being connected with the integration actualization.

Within the frame of the present conception there is also an opportunity to evaluate the organizational innovative work influence on the main activity. The degree of innovations influence on the potential of the aspect "Products" is mediated by the influence of innovations on the potential of every of the aspects "Finance, Resources" and "business-Processes". Such an influence on the aspects, finally, is expressed in the growth of that *part* of every of their *potentials*, which can be acknowledged to be "*innovative"* for a certain moment. In its turn, the growth of the innovative part of every potential is achieved by means of purposeful managerial impacts on the *realization* of the previous potential in the chain, primordially oriented to this.

The given perspective suits the task of marking out the innovative activity in the "production and commercial" and management activities of the participant with the possibility of further recording and analysis of:

a) its properly innovative activity development;

b) the degree of its influence on separate aspects of the "production and commercial" operations of the participant (their potential and development), including that on the final product (potential "Products");

c) the degree of its influence on the final product of the organization activity – the achievement of its strategic objectives and mission.

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Materials of Conferences

STUDENTS' SELF-INSTRUCTIONAL METHODOLOGICAL MATERIAL EFFICIENCY: "TRAINING SCHEME OF WORK-RELATED DISEASE OR OCCUPATIONAL HAZARDS PATIENT'S CASE HISTORY"

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The purpose of the present work has been the estimate of efficiency of the textbook of methodics for students: "Training chart of work-related disease or occupational hazards patient's case history", developed by the assistants of our Department on the ground of State Educational Standard requirements on discipline.

The discussed textbook has been created to teach students the features of work-related disease patients' or suspects' management and such patients' histories writing rules.

The textbook consists of the following sections:

1. Background information about the patient.
2. Occupational history.
3. Sanitary and hygienic characteristic of the worksite
4. Unbiased state of the patient.
5. Diacritical argument.
6. Clinical diagnosis of the disease.
7. Working capacity of the patient.
8. Plan of curative and preventive measures of medical nature.

A special attention is paid to the diacritical argument. The student should answer the following questions:

1. Which work-related diseases can occur owing to the influence of working environment hazards common for the worksite of a given patient?

2. Are there occupational disease signs? If there are some, then, which ones? To prove the occupational disease diagnosis or the lack of the last.

3. Is a given disease associated with the conditions of work (directly or indirectly)?

Further on, it is necessary to state a full explicated clinical diagnosis according to the modern classification, and in the absence of a complete examination of the patient - to evolve a plan of necessary laboratorial and instrumental surveys.

A big section is dedicated to the patient's working capacity evaluation. Concerning a given patient the student should determine if a temporary director or permanent disability (complete or partial one) takes place, if the provision of employment (redeployment) is necessary. Further on, a plan of curative and preventive measures of medical nature and sanitary and hygienic recommendations is evolved.

In the consequence of case history writing on the given scheme the students, first of all, master their professional skills (of patients' physical examination). Besides, when writing the occupational history, a suspicion in terms of possible association of the present disease with the occupation is developed, that is necessary in the following work of the doctor of any speciality.

At the work on the case history of a work-related disease suspect the student faces a concrete clinical situation distinct from those occurred earlier.

It develops an offbeat clinical thinking in the student, promotes a constructive and creative approach to the problem solution in any clinical situation.

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METHODOLOGY AND DEVELOPMENT OF EDUCATIONAL CULTURE IN DESIGN

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This article deals with innovative methods of teaching students-designers, which are based on using ornamentation as a basic element of shaping. Also the author of the article reviewed the principles of folk arts existing at the contemporary development level of society.

Teaching students to the shaping methods is on of the most important thing for designers profession. The lecturers start teaching them with an ornamental analysis of shape. Stylized design or transformation of natural motives is hardly the only way to teach students to shaping methods.

Why it happens?

Firstly, the ornamental structuring is the simplest and clearest to explain. It is a straight and spotty motif handling, shadowgraph emphasis and capability of ornamental handle, methods of composite drawing and graphic simulation. All of them help sequaciously and consistently passing on creation of new ornamental motif, not on shape, but ornamental motif.

Secondly, the composite principles are easier to treat on the ornamental composition, because it is clear and visual. The principle of three-component, intersubordination to integrity, consistency and simplicity are down visually and simply to the patterns pf 3 or 5 plane ornamental elements.

Thirdly, it is easier to convert the shape, we offer the variants aesthetic perception pf the shape and

are fascinated with its sculptural characteristics, multiplicity of straight handling, wonder proportional designs, i.e. decorative components. We don't create a new shape, but modernize an old one.

But in the result we should continue with the main, i.e. using an association circuit and converting shape further we should make them to imagine the shape without any forcing, just supported by the personal concepts and favors at perception of any natural motif. At this point we create a new style and also make authors attitude to the shape.

In this case the lessons' organizing depends on a design objective. For instance, in the first instance a shape stylized design isn't accompanied by the task to learn to find out its plastic characteristics in its simplified handle, etc. All their observations they should present in the sketch-pastiche, which emphasize the peculiar tasks of each of them, a line-plastic plane design of natural motif. A structure is its geometric shapes and proportional features of the motif.

It is necessary to overdo educed volumes that help to create a peculiar logic of link shape elements, to educe a unique trait and form personal idea of plastic characteristics of the natural motif. Finally, it allows creating constructive model of the natural motif. by means of transfusion of the shape peculiarities by presenting them in different stuffs: metal, glass and wood.

It's important to place emphasis on the fact, that at this point a technical training of a student is very important. Topside is a connection with disciplines for composition, by means of which we hone general principles and rules of visual harmonization of the elements, and drawing, which allows easy reading student's idea in the draft. Grasping of vivid and sharp expressiveness will help students to catch a spirit and to transfuse emotional features of the shape. A good drawing is an underlying basis of any constitutive activity, because the contemporary technical methods such as Photoshop or Corel DRAW, 3D max allow entering demote of an unique kind of create activity. It means that knowing IT and computer programs is an important aspect of the studying process. [1]

Let's hark back to the architectonic drawing. In the first instance the students think that the model image is in the up-and-doing usage of a handle. But this doesn't educe construction and practicability of stylized motif. That is why the lecturers often corrobate tasks by mottos, which allows directing student's activity to the constructive tasks solution.

These mottos are taken from composite principles: integrity, graininess, symmetry, asymmetry, dynamics, static, etc. In order the student could get the clearance of functional shape production at the final stage, it should pass away considerable amount of time. The general tasks of such work are a simple contour educing, perfect proportion defining from the point of view of visual analysis, coherence of stylized motif element. This work is important and even necessary in order the future designers know the process hornbook and could define themselves the way and methods of project searching.

But as it turns out there is easier way of shape searching. It is an ornament.

In course of time the ornamentally stylized nature took shape of functional frames, containers, headdresses, musical instrument and architecture. Here the shape and ornament merged in the unitary harmony and couldn't exist without each other. The research of Kazakh material culture and many other nations allows to conclude as follows: firstly, the ornament, which is the way of decorating, at bottom is more complex and important basis of any world style of the art and material culture.

Secondly, at the heart of any ornament is the mathematical precision of the motives, proportional coherence of the shapes and volumes, exact scheme of constructing elements of the ornamental schemes were basis of order systems in the ancient Greece.

Studying and using of the ornament in the project methods, a student is supplied with a ready composite material to solve the complex project tasks. You don't need to get long way over from studying of the natural motif to its stylized and turning out to the ornament. You need to be able to use the ornament as a basic one to form in the design. However by no mans the previous knowledge should be neutralized, but the thing is vice versa, they help to hasten the project process. It is very important in the guillotine of work act and life process.

Any national ornament has been designed for Ages. The natural motives form the peculiar correlations of gross geometric volumes (macrostructure) with little ones (microstructure). They are built on the principle of shape harmonization. The proportional correlations of the parts, their configuration poses a special module for further its modernization into functional form. This means that in the point we have a ready composite scheme to create a new design objective. There is nothing to do but we apply this scheme to take a decision in favor of shape functional features.

The general stages of work with ornament for studying shaping methods are the followings:

Educing ornamental structure is the work with the ornamental motif at the module net. The next stages are finding out of different variants of contingence for searching an emphasis shape contour and its variants; an accent defining and composite peculiarities of shape elements; accepting of composite schemes according to functional and aesthetic peculiarities of shape; shape draughting on the basis of made composite scheme.

The suggested method is put up so that it can give students the clear ideas of the system of interaction between art and life. It foresees a participation of the students' experience, also using widespread historic experience of many nations. Their development was in different historic epochs and in different direc-

tions, connected with objective conditions of people's existing. The problems of national peculiarities are directly connected with the problem of customs and innovation in contemporary art. The academicism features, national peculiarities and the sense of a new-build certainly develop a tendency to appear an artist-designer creative work and by no means don't come into antagonism with each other. If the ideas of an artist are progressive ones and he speaks sincerely at short notice and without preconceived thought, he knows well and feel root his own national culture and achievements of the world experience. To the extent that an artist takes into his head to make a national thing anyhow, combine rational the separate traditional elements with the modernity features, a remote and heartless stylizing succeeds. And the thing doesn't turn out modern and national. An artist's journey should be based on a creative putting into practice, which is conformable to the national features, not a mechanical wattage into the present-day life the artistic forms created long ago.

Therefore a topicality of this method is due to the following: there is a necessity of solving the problem of a lessons learned succession of the art experience, lessons learned by the folk craftsman generation, which is directly connected with a field of art education. An acquisition of theoretical and practical skills of contemporary design is very important. It possesses a rich arsenal of project and structural methods, the cultural significance of which is shown in the objective sphere organizing, synthesis of different art kinds, including an applied art. Meaning that it is directly relevant to succession, style forming processes based on the cultural customs. It allows implementing practical design more effective. [3]

The work objection is an establishment of the historically formed patterns of a composite construction of craftwork (weaving, metal- and leatherworking, etc.), defining of their connection to peculiarities of a trade education specify at Innovative University of Eurasia in order to implement and usage of methodic, graphic and semantic systems, which are peculiar to the folk art in contemporary designers' works.

Based on principle that the ornament is tried-and-true, adjusted system of the elements, which form a certain rhythmic order, one can conclude that the ornamental element is also a tried-and-true structure. Its complex plastic features of the natural motif are set by means of simple geometric volumes. As a result we have a simple composite scheme, which doesn't need to try the rules of composition. It is needed just to lead to the idea of practical, logic and constructive decision.

Knowing of sources, development of traditional crafts, knowing of history of the native country and world heritage of design is very important aspect of professionalism of the future designers. Today at the Age of a rising tide of interest to the historical roots, extend and at a new level studying of the folk art should become a part of an obligatory program.

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Materials of Conference

RISK EVALUATION OF THE ENVIRONMENTAL POLLUTION INFLUENCE ON THE POPULATION HEALTH IN URAL URBAN DISTRICT

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Health problems of the Ural Region population are largely associated with the environmental technogenic pollution defined by the industry impact, nonferrous and ferrous metallurgies, first of all. The territories of such manufacturing towns of the Ural Region as Kamensk-Uralsky, Krasnouralsk, Nizhnyaya Salda are referred to ecologically unfortunate ones. For the solution of the towns' ecological problems the development of Ecological Programs making the municipal government policy in the environment protection sphere and oriented to the Territory's ecological state improvement and people's invigoration are contemplated. The purpose of the work has been the scientific substantiation of the main directions of health optimization of the population living in the ecologically unfortunate territory. For the achievement of the stated objective the following problems were solved: the population health state estimation; the estimation of the population health cancerogenic risk from the chemical substances polluting the environment and planning ecological program priority measures aimed at the population health state improvement. The carried out investigations testified that the leading medium being hurtful to the health of the population is the contaminated open air. The analysis of air contamination with cancerogenes testifies that the volumes of individual cancerogenic risk in the territories of Krasnouralsk, Kamensk-Uralsky and Nizhnyaya Salda are at the level of 10^{-3} и 10^{-4}, that is typical for many large industrial cities of Russia. The leading position among the cancerogenes is occupied by benz (a)pyrene, chrome, nickel – in Kamensk-Uralsky; arsenic compounds – in Krasnouralsk, and formaldehyde – in the city of Nizhnyaya Salda. By virtue of the results of the carried out investigations a plan of measures on the population health rehabilitation and environment enhancement was formed.

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