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Background: Cystatins are natural endogenous inhibitors of cysteine proteases universally involved into development of different tumors. Tumor growth and metastazing include increased consumption of these inhibitors, followed by decreased level of cystatins and dysregulation of proteases/protease inhibitors system. However, the biological role of individual cystatins is still not clear. The most known cystatin C was shown to relate to some types of tumor development. Cystatins include a group of intracellular cystatins (belonging to type 1) and extracellular cystatins (type 2), among them cystatins C, D, E/M, F, G, S, SN and SA, which functions were not studied enough. It was suggested that cystatin SN was responsible in regulation of tumor growth locally.
The aim: To investigate cystatin C and cystatin SN concentrations in biological fluids of patients with intraocular melanoma as tumor biomarkers and possible therapy targets.
Materials and methods: The patients with melanoma chorioidea (57 patients; among them woman 36, men 21; aged from 28 to 80, of middle age of 56.6 ± 2.4 years) were under investigation. In all cases the pathological process involved one eye. The control group consisted of 37 healthy persons (volunteers), medical personnel in clinic and students, aged from 20 to 49 years; the middle age 31 ± 4.1 years); 7 patients with age-related cataract aged from 57 to 80 (middle age 71 ± 2.6 years; man 3, woman 4). The biological fluids studied: tears, intraocular fluid (obtained during operation) and blood serum. In all cases investigation was made according to informed agreement of patients and control group members. Cystatins concentration was measured by ELISA kits: for Cystatin C (BioVendor, Chechia) and for cystatin SN with help of Human Cystatin SN (CST1) Elisa Kit Cusabio, China. Statistical analysis was made by non-parametric statistic test of Kruskal–Wallis, for correlations – Spearman test. The difference between groups studied was considered significant $p < 0.05$.
Results: Increased serum level of cystatin C was revealed in patients with melanoma chorioides (1023.5 ± 78.9 ng/ml, $p = 0.019$) compared with the control (809.9 ± 146.8 ng/ml). In tears of patients with melanoma chorioidea, cystatin C concentration (441.7 ± 14.5 ng/ml) had a tendency to increase as compared to the data obtained in tears of the control group (287.5 ± 20.01 ng/ml) as well as the cystatin C level of intraocular fluid of these patients vs the control group ($p < 0.1$). Cystatin SN concentration in serum of patients with melanoma chorioidea (1.45 ± 0.30 ng/ml) was lower vs the control group (3.12 ± 0.32 ng/ml, $p = 0.0038$), as well as Cystatin SN level in intraocular fluid (1.43 ± 0.10 ng/ml) vs the control (2.60 ± 0.60 ng/ml, $p < 0.05$). There was no difference in cystatin SN concentration in tears of patients and control group.
Conclusion: In serum of control (healthy) group, cystatin C concentration is significantly higher than cystatin SN level in serum, tears and intraocular fluid. The reverse correlation was revealed between the level of these inhibitors in serum, that is suggested their possible interaction. In melanoma patients the reciprocal changes in cystatin C and cystatin SN were shown: increased cystatin C and decreased cystatin SN level in all biological fluids studied. On the basis of cystatins distribution in biological fluids of patients one can suggest their involvement in pathological process as system reaction of organism on tumor development.

http://dx.doi.org/10.1016/j.ejcsup.2015.08.024

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Genetic testing in early diagnostics and prevention of gastric cancer

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Background: To determine diagnostic importance of DNA methylation in patients with chronic atrophic gastritis and induction of "Correa" cascade for gastric cancer prevention.
Material and methods: This present study included 80 patients with chronic atrophic gastritis associated with *Helicobacter pylori*. Diagnoses were confirmed by endoscopic, morphologic, serologic examinations. Age of patients varied from 17 to 78 years old. There were 52 (65%) males and 28 (35%) females. The control group consisted of 32 patients with morphological verified diagnosis of stage I–II gastric cancer. Examination with the purpose to determine hypermethylation of DNA was performed simultaneously in biopsy materials and blood plasma. Provoking factors of hypermethylation in 4 tumors' genes, APE, E-Cadherin, T1MP3, hMLHI were determined by quantitative methylation with use of Polymerase Chain Reaction. To evaluate the level of methylation we compared the analysis' results of biopsy and blood plasma tests. Blood serum samples and biopsy specimens were collected at diagnosis until the therapy is started. All patients with chronic atrophic gastritis infected with *H. pylori* underwent anti-*H. pylori* therapy according to the protocol. Chronic atrophic gastritis was found at morphologic examination in 40 (50%) patients according to "Correa" cascade. 36 (45%) patients had intestinal metaplasia, and 4 (5%) patients had dysplasia. Reaction was considered to be positive in cases, when the level of methylation in genes listed above was higher in blood serum than in biopsy materials.
Results: High concentrations of methylated APE, T1MP3 and hMLIH in genes were found in blood serum of 8 (10%) patients. In the control group, all 32 patients with gastric cancer had high methylation level in blood serum. In the remaining 72 (90%) patients, no high concentration of DNA methylation was found. After the 2-nd course of anti-*H. pylori* therapy, patients underwent morphologic and endoscopic examinations according to the protocol. Eradication of *H. pylori* was determined in 86% patients who received therapy. Intestinal metaplasia decreased from 45% to 25% (20 patients). Mild dysplasia was found in 1.2% of cases. Repeated analysis of methylation level showed its decrease after anti-*H. pylori* therapy in 4 (50%) out of 8 patients.
Conclusion: Genetic tests show that DNA methylation in patients with chronic atrophic gastritis has high diagnostic importance. Anti-*H. pylori* therapy at the different stages of

"Correa" cascade has high level of induction in transforming into non invase gastric cancer.

http://dx.doi.org/10.1016/j.ejcsup.2015.08.025

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Epidemiology of malignant neoplasms of the oral cavity and pharynx in the territory of the Chelyabinsk region

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The Chelyabinsk region is a classic example of the technologically-saturated region. The index of pollution of atmospheric air is estimated as high. The Chelyabinsk region is among the areas of increased cancer risk. The incidence of head and neck cancer is steadily increasing, accounting for 20–25% of all cancer cases in Russia. Oropharyngeal cancer makes up 5.1% of all cancers.

Materials and methods: The object of the study was the population of the Chelyabinsk region. The analysis was conducted according to the materials of the annual reports of the statistics department of the Chelyabinsk district oncology dispensary.

Results: Out of the total cancer cases for the population of Chelyabinsk region in 2014, oro-pharyngeal cancer comprised 2.06%, including cancers of the lip (0.35%), tongue (0.47%), major salivary glands (0.22%), other unspecified parts of the mouth (0.52%), oropharynx (0.33%), nasopharynx (0.1%) and hypopharynx (0.07%). From 2008 to 2014, the incidence of oral and pharyngeal cancer among adult population of Chelyabinsk city and Chelyabinsk region showed an 8.8% increase. In the period from 2011 to 2014, the incidence of oral and pharyngeal cancer tended to increase, the overall rise being 71.8%. It should be noted that the oral and pharyngeal cancer incidence was 3 times higher in males than in females in 2013 and 2 times higher in 2014. One of the main indicators that determine the prognosis for the development of cancer, is the extent of tumor at time of diagnosis.

Out of the total cancer cases for the population of Chelyabinsk region in 2014, cancer of the oral cavity comprised 1.33%, pharyngeal cancer 0.6%, lip cancer 0.13%, ranking the 17th, 19th and 24th place respectively among the causes of death from all cancers. Analyzing the dynamics of mortality from cancer of the oral cavity and pharynx during the study period, it was revealed that the mortality rate increased by 0.7%.

Conclusion: Head and neck tumors are a rare group of clinically and biologically diverse neoplastic diseases. Among the residents of the Chelyabinsk region, men are 2–3 times more susceptible to cancer of the oral cavity and pharynx than women. High mortality rate is due to late referral of patients to specialized clinics; most head and neck cancer patients are diagnosed at advanced stages.

http://dx.doi.org/10.1016/j.ejcsup.2015.08.026

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Biochemical markers and clinical symptoms in pancreatic cancer patients

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Background: To evaluate the clinical symptoms in pancreatic cancer patients (PCa) and compare some biochemical blood serum parameters in patients with different pathology of the pancreas (PCa, acute (OP) and chronic pancreatitis (CP)).

Materials and methods: During a one-time clinical research on the type of "series of cases" 130 patients were examined (42 patients with OP, 81 – CP and 7 patients with PCa). The diagnosis of PCa, OP, CP was verified by clinical and instrumental methods. Glucose, cholesterol, triglyceride and bilirubin serum levels were determined by ELISA.

Results: The mean age of patients with PCa was 63.6 ± 4.9 years, morbidity duration of PCa – 3.5 ± 1.1 months. Among patients with PCa, 83.3% of people – smoked, 16.7% – smoked every day. Half of the respondents PCa patients noted that over the last year they did not drink alcohol; 16.7% of people – drank alcohol several times a year, and 33.3% of patients consumed alcohol 1–2 times a month. BMI of PCa patients was equal to 26.3 ± 3.5 kg/m^2, in OP patients – 23.8 ± 1.0 kg/m^2, in CP patients – 26.3 ± 0.6 kg/m^2, $p > 0.05$. In this case, 85.7% of PCa patients noted a significant decrease in body weight (11.7 ± 6.0 kg) for 3–4 months after the onset of symptoms. There was no pain in 42.8% of PCa patients, and frequent pain noted only in 28.6% of persons. Among CP patients, frequent and persistent pain noted in 65.5% of patients and among OP patients in 48.6% of cases. All PCa patients experienced pain in the right upper quadrant. Pain was of low intensity in 75% of cases and moderate in 25% of cases. Elimination of pain was observed in half of the PCa patients, and 1/4 of patients continued to experience pain. Episodes of nausea and vomiting noted in 25% of PCa patients. Bloated feeling in the stomach and overflow were noted in 42.8% of the all surveyed PCa persons. The level of glucose in PCa patients exceeded the normal limits and was significantly higher compared to that in OP and CP patients (8.5 ± 1.4 mmol/L, 5.4 ± 0.3 and 5.1 ± 0.1 mmol/L, respectively, $p < 0.05$). Hyperbilirubinemia was detected in PCa patients – 89.9 ± 27.5 μmol/L; in OP and CP patients bilirubin levels were 32.2 ± 11.0 and 13.4 ± 1.8 μmol/L, respectively, which were significantly lower than those in patients with PCa, $p < 0.05$. Triglyceride levels did not differ in patients with different pancreas diseases (PCa – 1.7 ± 0.3, CP – 1.86 ± 0.1 and OP –1.88 ± 0.11 mmol/L, $p > 0.05$). However, the total cholesterol in CP patients was significantly higher than that in PCa and OP patients (5.8 ± 0.1, 5.0 ± 0.6 and 4.1 ± 0.2 mmol/L, $p < 0.05$). In PCa patients, the elevated levels of some markers of cholestasis and hepatocyte injury were also found: ALP – 185.0 ± 12.7 IU/L, ALT – 108.4 ± 33.5 IU/L, AST – 85.3 ± 31.5 IU/L, amylase – 44.9 ± 14.9 IU/L, fibrinogen – 2696.6 ± 398.6 g/L.