S.I. Kirkilevskiy, O.N. Sulaieva[3], A.A. Mashukov[1, 2], A.I. Rybin[1], O.A. Bilenko[1],
V.E. Maksimovskiy[1], D.V. Raciborskiy[2]
National Cancer Institute, Kyiv, [1]Odesa National Medical University, Odesa
[2]CHPI "Odesa Regional Oncological Center", Odesa, [3]Medical Laboratory CSD, Kyiv

MULTIFACTOR ANALYSIS OF THE ONCOPROTEINS EXPRESSION DEPENDENCE IN GASTRIC CANCER

e-mail: mashukster@gmail.com

The total of 26 patients operated on for gastric cancer in the period of 2007-2011 was included in the study performed on the basis of the Abdominal Oncology Surgery Department at the CHPI "Odessa Regional Oncologic Dispensary". In all cases, the so-called lymph node dissections were carried out based on principle considerations, i.e. extensive prophylactic biopsies of visually unchanged lymph nodes. A multifactor analysis of p53, VEGFR-3, Her2/new oncoproteins expression and Ki67 proliferative tumor activity dependence on the involvement of the tumor microcirculatory bed (ly, v), local growth (T), the presence of residual tumor tissue (R), the degree of tumor differentiation (G), the degree of regional lymph nodes involvement (N), the microinfiltration type (Inf α, β, Inf) was performed.

Key words: gastric cancer, immunohistochemistry, oncoproteins.

С.І. Кіркілевський, О.М. Сулаєва, А.О. Машуков, А.І. Рибін, О.А. Біленко,
В.Є. Максимовський, Д.В. Раціборський

БАГАТОФАКТОРНИЙ АНАЛІЗ ЗАЛЕЖНОСТІ ЕКСПРЕСІЇ ОНКОБІЛКІВ ЗА РАКУ ШЛУНКУ

Всього в дослідження, проведене на базі абдомінального онкохірургічного відділення КУ «Одеський обласний онкологічний диспансер», включено 188 хворих, оперованих з приводу раку шлунка за період 2007-2011 рр. У всіх випадках виконані т.зв. лімфодісекції з принципових міркувань – великі профілактичні біопсії візуально незмінених лімфовузлів. Проведено багатофакторний аналіз залежності експресії онкобілків p53, VEGFR-3, erbB2 і проліферативної пухлинної активності Ki67 від залученості пухлинного мікроциркуляторного русла (ly, v), місцевого зростання (T), наявності резидуальної пухлинної тканини (R), ступеня диференціювання пухлини (G), ступеня залученості регіональних лімфовузлів (N), виду мікроінфільтрації (Inf α, β, Inf Y).

Ключові слова: рак шлунку, імуногістохімія, онкопротеїни.

The study of connections between one and another histological and immunohistochemical markers expression is still largely speculative, theorized, remaining a "book science".

The population of tumor cells is inhomogenous, there are subpopulations of cells at different stages of the cell cycle, with different sensitivity to chemotherapeutic regimens [7]. Diffeences between chemonaive and pretreated cancers (formation of drug resistance) motivate to obtain repeated biopsies and stimulate gradual introduction of immunohistochemical studies not only of remote operating drugs, but also immunocytochemical study of tumor bioptates [1], including those in stomach cancer.

Introduction of gastric cancer molecular classification into the clinical practice [3], like the one that is widely used in breast cancer nowadays, makes this search direction topical.

A study on the expression of oncoproteins in stomach` carcinomas, has been turned into a real research basically due to the abundance of results and their comprehensive interpretations. The study was carried out at the abdominal onco-surgical department of Odessa Regional Oncology Center, included a study of patients operated on for gastric cancer (GC) within 2007-2011. In all cases, the so-called lymphadenectomy was performed for the principal reason of extensive preventive biopsy of visually unchanged lymph nodes. We performed a multivariate analysis of interactions between the expression of oncoproteins and micro involvement of tumor vasculature, the local growth, the presence of residual tumor tissue, the degree of tumor differentiation, the degree of regional lymph nodes involvement and type of infiltration.

An interesting observation is conducted by the workpiece varying the concept of "the degree of malignancy" or "degree of biological aggressiveness" depending on the combination of IHC markers. This can hardly be called staging, because due to the small size of the group we could not identify 3-4 groups in each of the VEGFR, p53, Her2/new, Ki-67 species. There are a number of reports on the prognostic role of Her2/new marker in gastric cancers [2, 4, 6, 9].

Therefore, the survival of a group seen as the Chief Arbiter of the aggressiveness of the cancer, making it a more "malignant" or, on the contrary more torpid and "benign". It was impossible in one study to consider all variants of protein molecules that are expressed in stomach cancer [8, 11].

The purpose of the study was to form an understanding of the cells changes holistic picture in gastric cancer by performing histological and immunohistochemical studies, genetic tests, as well as estimation of possibilities for further affecting a tumor by means of individualized programs of special, including chemotherapeutic, treatment.

Materials and methods. The present study included 26 patients who had been operated in the Municipal Institution Odessa Regional Oncologic Dispensary within in the period of 2011-2017. Histological, immunohistochemical (further IHC) and, in a number of cases, genetic properties of removed tumors were under study. Interest was drawn by both the quantitative study of this or that marker pronouncement in the population of patients with gastric cancer (GC), and the correlation between these three groups. The ultimate goal was to study the effect of markers expression impact on survival and to compare the survival rates of GC patients with combinations of marker characteristics.

The age of the patients ranged from 43 to 79 years, amounting the mean of 60–85 years. In the case of the cardia cancer, 3 persons (11.54 %) were operated on; 12 patients (46.15 %) were operated for the gastric cancer, 7 patients (26.92 %) – for the gastric body cancer, with tumors affecting the entire stomach –1 patient (3.85 %), in 3 more cases the tumors occupied more than one anatomical segment. Using the Microsoft Office Exel 12 program, the Spearman's rank correlation coefficient was calculated to assess the correlation pronouncement between the respective table values of the markers. The credibility of evidences was considered significant at $p < 0.05$, which was sufficient for mathematical verification of the findings in biological studies.

The obtained operating material was fixed in a 10 % solution of buffered neutral formalin. Biomaterial fixation (dehydration and paraffin impregnation) was performed in automated histoprocessors (Milestone LOGOS Microwave Hybrid Tissue Processor, Milestone, Italy). After fixation, the material was embedded in paraffin with the manufacture of paraffin blocks at filling stations and the manufacture of paraffin blocks Thermo Scientifis HistoStar (Thermo Fisher Scientifis, USA). Histological sections with a thickness of 4 μm were made on a semi-automated rotary microtome Thermo Scientific HM 340E. The preparations were stained with hematoxylin and eosin using an automated coverstainer Dako Cover Stainer (Agilent, USA). Histochemical staining was performed manually. The NIKON ECLIPSE E200 microscope (NIKON CORPORATION, Japan) was used for microscopic examination of the material.

Paraffin blocks were used for immunohistochemical staining VEGF-C (KLT reagent 9). Thin sections were prepared, which were treated with a solution of 0.3 % hydrogen peroxide for 10 minutes at room temperature. For antigen detection, the sections were treated with sodium citrate pH 6.0 and placed in a microwave oven. During 12 hours at 4°C in humid conditions, we observed processing of primary antibodies: goat polyclonal VEGF-C antibody [1: 100, Biotechnology Santa Cruz, Santa USA]. Then the sections were washed three times in phosphate buffer solution for 2 minutes, for 30 minutes at room temperature the solution was placed in horse reddish peroxidase (Envision, DAKO), labeled goat antibodies. There was added 3,3-diaminobenzidine. Normal goat IGG served as a negative control for the detection of VEGF-C. The degree of staining intensity was classified into four degrees: none (0), mild (1), moderate (2) and severe (3). Immunohistochemical staining procedure for the study of other markers differ almost only in the form of antibodies used: for the p53 – is a Do-7 [fig. 1.], m7001, DAKO, Glostrup, Denmark, for Her2/new [fig. 2, 3] – it is a 2-erB-Oncoprotein, Ki-67 – reagent MIB-1 [fig. 4.].
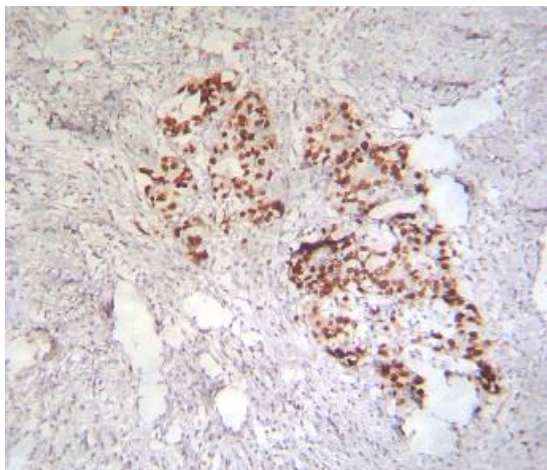

Fig. 1. Microphotograph. Immunohistochemical staining of p53 Protein (DO-7) – expression level of oncoprotein with the molecular weight of 53 kDa – 80 %. Magnification x100.
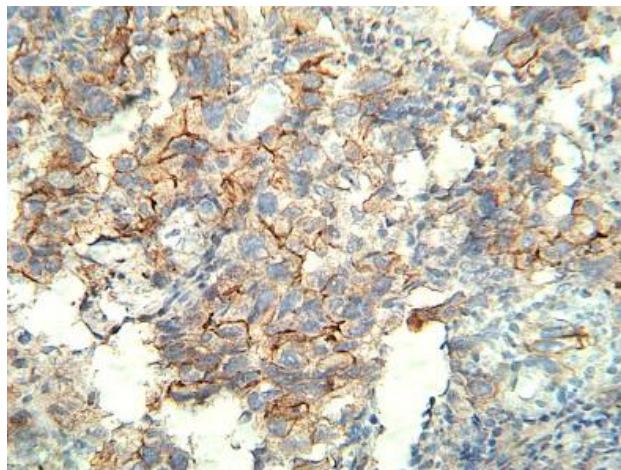

Fig. 2. Microphotograph. Immunohistochemical staining of Her2/new (c-erB-2 Oncoprotein) – "3+". Magnification x200.

Results of the study and their discussion. Most frequently, in the histological examination of the removed surgical material, the adenocarcinoma of the stomach was detected morphologically – 7 patients (26.92 %). In 5 cases, it was signet ring cell (colloid) carcinoma (19.23 %), in 6 cases (23.08 %) – mixed adenocarcinoma with signet ring cells. In 3 patients, the so-called adenogenic stomach cancer (11.54 %) was diagnosed. In 5 cases, more rare forms of GC (19.23 %) were reported: glandular solid, tubular-papillary, alveolar-solid, infiltrative-solid, and cribriform-acinic cancer.
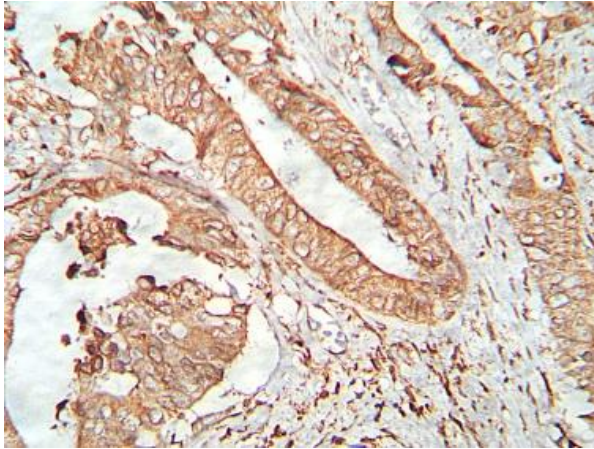

Fig. 3. Microphotograph. Study of Her2/new gene expression (c-erB-2 Oncoprotein): "+++". Magnification x100.
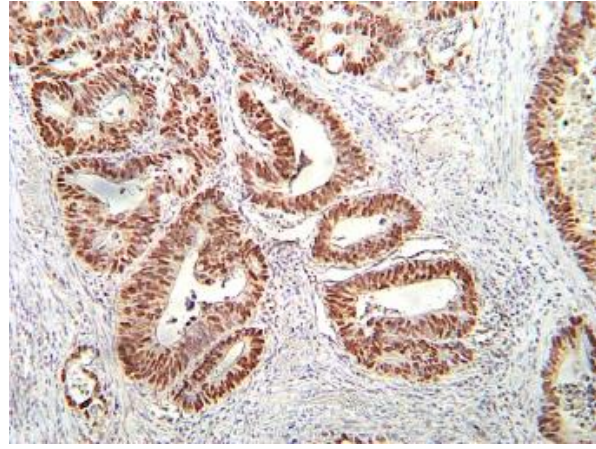
Fig. 4. Microphotograph. The image of tissue with the expression level of Ki67 Protein (MIB-1) is 80 %. Magnification x100.

In 3 cases among the above forms there was mucus production, bifocal cancer was observed, in 2 preparations there were tumor necrosis, in 4 patients in the removed tumors there was pronounced immune peritumoral reaction, lymphocytic infiltration. The type of tumor had a reverse correlation with the expression of topo2α, $r_{Pearson}$ = –74.67 %. In the patient population, there were 2 patients with morphological tumor structure features.

In 10 (38.46 %) cases there was a low-differentiated cancer (G3), in 2 (7.69 %) cases, highly differentiated cancer (G1), in 4 cases (15.39 %), the degree of differentiation was not defined (Gx) in the pathomorphological study, in one case (3.85 %), the removed tumor was represented by anaplasized undifferentiated carcinoma (G4). In 4 cases (15.39 %) a mixed moderately low-differentiated cancer (G2–G3), in 1 case (3.85 %) – a mixed high-moderately differentiated cancer (G1–G2) was observed. In 4 (15.39 %) cases, a moderately differentiated GC (G2) was detected.

A moderate correlation was observed between the degree of tumor differentiation (G) in the group and the expression of the Ki-67 marker ($\rho_{Spearman}$ = 51.59 %, $r_{Pearson}$=53.05 %), as well as a strong negative correlation with the expression of E-cadherin protein in the tumor. A weak (Spearman correlation coefficient ρ = 47.16 %) rank correlation between the degree of differentiation and the tumor/stroma ratio was revealed.

The size of the tumor in the stomach, measured by the morphologist, varied from 0.5 to 12 cm. The size of the tumor slightly correlated with the degree of regional lymphatic capillaries injury (ly, section 2.1.6.3.1, "lymphatic invasion", according to the Japanese classification: General Rules for Gastric Cancer Study, Japanese Research Society for Gastric Cancer, 3rd edition, 2011) – $r_{Pearson} = \rho_{Spearman}$ = 48.73 %. The rank correlation coefficient between the tumor size measured by the morphologist during the material cutting and the TS marker was high and amounted

$r_{Pearson}=\rho_{Spearman}$=79.32 %; a close correlation was found in this case with the number of metastasized lymph nodes, the correlation coefficient $r_{Pearson}=\rho_{Spearman}$=68.49 %.

During the operation, regional lymph nodes were removed, and the most frequently 16 lymph nodes were subject to removal. Dissection of the lymph nodes was of preventive and staging nature. It was most frequently performed in D2 volume. The number of lymph nodes removed, calculated in the gross specimen by the histologist, varied from 6 to 20. The mean number was m_o=13.19±3.10 removed lymph nodes.

Concerning the metastasized lymph nodes, their number among the removed ones ranged from 1 to 9 lymph nodes, averaging 2.12 lymph nodes, while there were no metastasized lymph nodes at all (classical preventive lymphadenectomy) in 9 patients (34.62 %).

The high ($\rho_{Spearman}=r_{Pearson}$=–74.43 %) reverse correlation was observed between the number of metastasized lymph nodes in each particular case with the ERCC1 marker: i.e. the more pronounced its expression was, the smaller was the number of affected regional lymph nodes.

Monoclonal antibodies are already available for a wider study of microsatellite instability in gastric cancer (GC):

Mismatch Repair Protein (MLH1) – ES05 antibodies

Mismatch Repair Protein (MSH2) – 25D12 antibodies

Mismatch Repair Protein (MSH6) – PU29 antibodies

Mismatch Repair Protein (PMS2) – M0R4G antibodies.

All the above means that this direction is promising for analysis, not even in the laboratory, but in the field clinical conditions.

Immunohistochemical studies were performed to assess the degree of p53, VEGFR-3, Ki67 [5], Her2/new protein products expression [10]. One of the most important facts about Her2/new expression in gastric cancer is a milder approach to recognizing the marker as positive, compared to breast cancer. In our study, the "++" marker was considered positive. While for breast cancer, the "+++" criterion is necessary.

Promising, but not included in our research, is the Her1 oncoprotein or EGFR as it is called today. We have one observation of GC with a mutation of this gene and expression of the respective protein product.

The distribution of GC patients with the expression of various factors was interesting from the point of view of the severity of one or another marker in groups. The p53+(49.52 %), VEGFR-3+(43.56 %), Ki67 +(33.33 %), Her2/new+(62.22 %) oncoproteins of patients had a high and moderate degree of histological differentiation of all IHC tests having positive expression.

A high level of erbB2 specifically for this enrolled set of patients was a synonym of a less aggressive course in contrast to the other three indices. Almost the same as for breast cancer, Her2/new+ unlike triple negative cancers, was still a more favorable form of the course (Her2 genetic type of breast cancer, along with luminal A and B types).

The calculation was performed not to all pateints, but only of all positive ones, and then of all negative ones. The p53– (22.89 %), VEGFR-3– (35.63 %), Ki67– (65.79 %), Her2/new – (34.96 %) proteins of patients had a high and moderate degree of histological differentiation, of all IHH tests that had no expression at all. Research is sometimes associated with the fact that some results cannot be explained at all, or there is lack of data.

For example, it is clear why the mitotic index in most of the g1+g 2 patients was less than 30. Such tumors divide more slowly, progress more slowly, and therefore are more "benign". It is obvious that due to the low aggression potential, there were fewer patients with VEGFR-3 positive tumors. The same applies to another "genetic instability factor" - the p53 protein.

The p53 + (50.48 %), VEGFR-3 + (56.43 %), Ki67 + (66.67 %), Her2/new + (37.78%) proteins of patients had a low degree of histological differentiation or its absence in all the IHC tests having a positive expression (*unfavorable prognosis*). More aggressive, low-differentiated tumors accumulated more p53, VEGFR-3 proteins and had much worse mitotic activity.

IHC test is not a genetic one, and it cannot be used to assess the mutability degree of p53, for example, and to determine what particular mutations are taking place. Immunohistochemistry gave indirect information. If p53 protein becomes abundant, then there is an increased expression of the TP53 gene. This could be used along with the usual histological markers.

The p53– (77.11 %), VEGFR-3– (64.37 %), Ki67– (34.21 %), Her2/new – (65.04 %) proteins of patients had a low degree or complete absence of histological differentiation of all the IHC tests having no expression at all. In the group of negative marker values, the greatest impression was made by the fact that the absence of erbB2 coincided with the tumor anaplasia.

Regarding the markers Her2/new and VEGFR, their expression was most frequently negative and the practical significance of their assessment was important for the purpose of prescribing adjuvant special therapy with trastuzumab and bevacizumab to the gastric cancer patients in the postoperative period. Monoclonal antibodies CB11 were used to assess the Her2\new expression in the tumor. Positive Her2\new was detected in 4 patients out of 26, with its strong expression revealed in 3 patients (3+, +++) and in one patient – 1 "+". It was a weak correlation, $r_{Pearson} = 41.68$ % with the presence of perineural tumor growth.

The VEGFR marker is heterogeneous in composition and its practical significance is represented by its 2 fractions: VEGFR1 and VEGFR3. VEGFR1 was a marker of sensitivity to sunitinib therapy, and VEGFR3 could characterize "neolymphangiogenesis" in terms of the neolymphatic capillaries formation in the tumor.

To assess the expression of $VEGFR_3$ in the tumor, monoclonal antibodies KLT-9 were used and to assess $VEGFR_1$ VG1 was applied. Below we tried to trace whether there was a link between VEGFR

expression and the presence of: a) perivascular tumor growth; b) the presence of extravasates and tumor emboli in the lymphatic and venous type vessels; c) the severity of lymphogenous metastases in paragastric collectors, including the Will Rogers phenomenon.

Ki-67 varied from the completely negative expression value, the minimum value of positive expression was 10 %, the maximum – 90 %. To assess its expression in the tumor, IHC reagent MIB-1 was used. The level 0–9 was observed in 3 patients, 10–19 were observed in 3 patients, 20–29 – in 5 patients, 30–39 – in 2 patients, 40–49 – in 6 patients, 50–59 - in 3 patients with GC, 60–69 - in 3, 70–79 – in 1, 80-89 – in 0, 90-99 – was not observed. The mean value of Ki-67 marker expression in the group amounted: $m_o = 33.35 \pm 20.54$.

Using the Microsoft Office Exel 12 software, the Spearman correlation coefficient has been calculated to assess pronouncement of the correlations between the corresponding table values of the markers.

The marker correlated with the expression of p53 ($\rho_{Spearman}$=63.83%), TS ($\rho_{Spearman}$ = -51.81 %), the differentiation degree G ($\rho_{Spearman}$=51.59 %, $r_{Pearson}$=53.05 %), the type of wall infiltration (abbreviation INF by the Japanese classification), $\rho_{Spearman}$ = -59.78 %, topo2α$r_{Pearson}$=47,08 %, ERCC1$r_{Pearson}$= − 47.82 %.

Today, standardization and implementation of precision medicine are equally important in oncology. Optimization of tactics and methods of treatment of patients with resectable gastric cancer by personalization of drug therapy and individualization of surgery has been in priority focus of specialists, but mostly remains an unresolved issue. Precision, or personalized, drug therapy, compared to standard, increases the chances of improving patient survival and medical aspects of their quality of life. It is already an important component of medical cancer treatment, even more is expected from new and future targeted drugs.

The cytological and histological part of the study included several indicators, including type of microscopic infiltration and the clarity of the border of growth in the surrounding tissues – INF; lymphatic invasion of tumor – ly; venous invasion – V; residual tumor disease – R; histological phenotype. The immunohistochemical panel had the following markers: Ki-67, p53, Her2/new, VEGFR (mandatory group, VEGFR-1 or VEGFR-3). The goal of the work is to clarify the value of laboratory and research data used in the daily practical work. The collected and generalized material presents a modern and comprehensive approach to multifactor analysis of tumors using biological technologies that have become available in Ukraine over the past few years.

For the first time, during the work, it was shown that there are at least several biologically heterogeneous types of cervical cancer, which are characterized by different aggressiveness, with different immunohistochemistry, cytohistology and different predisposition to neoangiogenesis, perineural invasion, emboli in tumor MCR, etc. [2, 4, 6, 9]

There were at least 2 pairs of markers (VEGFR-3/R and Ki-67/R), which actively correlate with each other with a correlation force of 0.994. Odds ratio (OR) for combinations of markers T/p53 = 27,108, p53/V =6,452, VEGFR-3/Inf=5,643, VEGFR-3/T=21,111, VEGFR-3/V=512,071, p53/T 27,108 , Ki67/Inf = 7,894, Ki67/V=53,935, Ki67/R=26,875, VEGFR-3/R=7,933, T/VEGF=21,111 significantly more than 1; which is more typical not for medical and biological research projects, but for the mathematical accuracy of physical and technical sciences.

The research presents the results of our own studies of surgical-pathohistological parallels, made intermediate conclusions that the search for new molecular prognostic factors is required, because metastatic lesions of the tumor microcirculatory tract could not be determined by the patient before surgery [1, 3, 7]. All patients included in the study have been operated, tumor, removed during surgery, was examined using immunological, histological, cytological, immunohistochemical methods. The results obtained in terms of the presence and absence of statistical parallels and mathematical correlations between the studied markers are traced.

Gastric cancer is an extremely biologically diverse disease. The obtained results allow to position the work as a study of the clinical biology of gastric cancer.

Conclusions

1. The modern rapid molecular genetics development of oncological science creates prerequisites for a more individual impact on the tumor.

2. The abundance of immunohistochemical and genetic data obtained during the patients examination, eventually will result in a deeper understanding of the gastric cancer biology, including the planning of surgery in a particular patient.

References

1. Amato M, Perrone G, Righi D. HER2 Status in Gastric Cancer: Comparison between Primary and Distant Metastatic Disease. Pathol Oncol Res. 2016; 30: 1–7.

2. Ananiev J., Gulubova M., Manolova I., Tchernev G. (2011). Prognostic significance of HER2/neu expression in gastric cancer. Article (PDF Available) in Wiener klinische Wochenschrift 123(13-14):450–4.

3. Chen T, Xu XY, Zhou PH. Emerging molecular classifications and therapeutic implications for gastric cancer. Chin J Cancer. 2016 May 27; 35(1):49. doi: 10.1186/s40880-016-0111-5. Review. PMID:27233623.

4. Gravalos C.; Jimeno A. (2008) HER2 in Gastric Cancer: A New Prognostic Factor and a Novel Therapeutic Target. Ann Oncol. 19(9):1523-1529 (повнотекстова).

5. Huang G, Chen S, Wang D, Wang R, Lin L, Chen S, Wang L, Huang Q. High Ki67 Expression has Prognostic Value in Surgically-Resected T3 Gastric Adenocarcinoma. Clin Lab. 2016; 62(1-2):141–53.

6. Jørgensen J. T., Hersom M. (2012) HER2 as a Prognostic Marker in Gastric Cancer - A Systematic Analysis of Data from the Literature. J Cancer 3:137–144. doi:10.7150/jca.4090 (повнотекстова).

7. Kanayama K, Imai H, Yoneda M, Hirokawa YS, Shiraishi T. Significant intratumoral heterogeneity of human epidermal growth factor receptor 2 status in gastric cancer: A comparative study of immunohistochemistry, FISH, and dual-color in situ hybridization. Cancer Sci. Apr. 2016; 107(4):536–42. doi: 10.1111/cas.12886. Epub 2016 Feb 19.

8. Nadauld L.D., Ford J.M.. (2013) Molecular profiling of gastric cancer: toward personalized cancer medicine. J Clin Oncol. 31(7):838–839. doi: 10.1200/JCO. 2012.47.1714.

9. Rüschoff J. (2012) HER2 testing in gastric cancer: a practical approach. Modern Pathology 25, 637–650.

10. Sheffield BS, Garratt J, Kalloger SE, Li-Chang HH, Torlakovic EE, Gilks CB, Schaeffer DF. HER2/neu testing in gastric cancer by immunohistochemistry: assessment of interlaboratory variation. Arch Pathol Lab Med. 2014; 138(11):1495–502. doi: 10.5858/arpa.2013-0604-OA.

11. Stahl P, Seeschaaf C, Lebok P, Kutup A, Bockhorn M, Izbicki JR, et al. Heterogeneity of amplification of HER2, EGFR, CCND1 and MYC in gastric cancer. BMC Gastroenterol. 2015; 15:7.

Стаття надійшла 10.03.2020 р.

O.I. Koval
Bogomolets National Medical University, Kyiv

RELATIONSHIP BETWEEN FACTORS IN REGULATION OF CHILDREN'S BEHAVIOR AND THEIR DENTAL STATUS

e-mail: Okoval78@ukr.net

A child's health is based on his upbringing. The child's behavior at the dentist's visit, the child's attitude to oral hygiene: all this reflects the behavior of parents in family relationships and their attitude to dental health in general. The pediatric dentist must take into account the peculiarities of the style of parental upbringing to achieve the aim of forming a positive attitude to the child's dental treatment in the future. The article presents the results of determining the dental status of children depending on the main forms of parenting style. According to the results of dental treatment, the choice of conditions for dental rehabilitation is substantiated and the influence of parenting style on the formation of dental health in children is studied.

Key words: children, oral hygiene, parenting style, dental caries, "parental love", "parental control".

О.І. Коваль

ВЗАЄМОЗВ'ЯЗОК МІЖ ФАКТОРАМИ РЕГУЛЮВАННЯ ДИТЯЧОЇ ПОВЕДІНКИ ТА СТОМАТОЛОГІЧНИМ СТАТУСОМ ДІТЕЙ

В основі здоров'я дитини лежить її виховання. Поведінка дитини на стоматологічному прийомі, ставлення дитини до гігієни порожнини рота – все це відображає поведінку батьків у сімейних стосунках та їх відношення до стоматологічного здоров'я в цілому. Лікарю стоматологу дитячому необхідно враховувати особливості стилю батьківського виховання для досягнення мети у формуванні позитивного ставлення до стоматологічного лікування дитини в майбутньому. В статті представлені результати визначення стоматологічного статусу дітей залежно від основних форм стилю батьківської поведінки. За результатами стоматологічного лікування обґрунтовано вибір умов проведення стоматологічної санації та вивчено вплив стилю батьківської поведінки на формування стоматологічного здоров'я у дітей.

Ключові слова: діти, гігієна порожнини рота, стиль виховання, карієс, «батьківська любов», «батьківський контроль».

The issue of dental health of the nation remains a topical issue today and fully depends on the dental health of children, especially their dental education.

The dentist's cooperation with children involves communication not only with the patient, but also with his parents (guardians), because they are the most important people for their children, especially in those years when the child's personality is still being formed. It is known that the dental status of the child,