

metacarpal bone distraction device shown imposition developed clinic.

2. The use of MLC can achieve solid fixation of bone fragments during the treatment period, sufficient for the early development of movement in the adjacent joints and contributes to a significant reduction in terms of hospitalization and total disability. Use of BWW will shorten patient treatment for all kinds of damage in 2 times and total disability period of 4–5 days.

3. Surgical interventions carried out at the turn of the distal end of the metacarpal bones, must be accompanied by a complex post-operative rehabilitation.

4. The application of distraction apparatus for treatment of fractures of the metacarpal bones of the hand, allows you to get excellent and good outcomes in 83.1% of patients, which gives reason to recommend it for widespread use in the practice of medical institutions.

References:

1. Устройство для разработки и лечения при повреждении суставов пальцев/№ FAP 00523 24.02.2010 г.
2. Асимова С. У., Хайдаров А., и соавт. Переломы пястных костей кисти и их лечение Вестник ТМАН № 2/2012 С. 50–52.
3. Асимова С. У., Хайдаров А., и соавт. //Применение дистракционного аппарата при переломах пястных костей кисти //Гений ортопедии № 3/2012. С. 15–19.
4. Бейдик О.В, Островский Н.В, Шевченко К.В, Левченко К. К. //Топографо-анатомическое обоснование чрескостного остеосинтеза коротких трубчатых костей кисти. Гений ортопедии 2006 № 2. С. 18–21.
5. Голобородько С.А. //Лечение несвежих переломов шейки пястных костей стержневым аппаратом наружной фиксации. Вестник травматологии и ортопедии им. Н. Н. Приорова 2002. № 1. С. 70–72.
6. Информация. //Современные технологии диагностики, лечения и реабилитации повреждений и заболеваний кисти (международная научно-практическая конференция). Вестник травматологии и ортопедии им. Приорова Н. Н. 2006 № 1 С. 94–95.
7. Кляквин И. Ю., Мигулева И.Ю, Охотский В. П. //Травмы кисти //2009. С 150–186.
8. Козьмина Т.Е, Знаменская М. Г. //Оценка функционального состояния кисти после проведенного лечения методом чрескостного остеосинтеза. Гений ортопедии 2002. № 3. С. 77–79.
9. Коршунов В. Ф., Магдиев Д.А, Барсук В. И. //Стабильный интрамедуллярный остеосинтез при переломах пястных костей и фаланг пальцев кисти. Вестник травматологии и ортопедии им. Приорова Н. Н. 2000 № 2. С. 22–26.
10. Мусалатов Х., Юмашев Г., Силин А. //травматология и ортопедия //2007.
11. Rolando S. Clin Orthop Relat Res //Fracture of the base of the first metacarpal and a variation that has not yet been described: //1910. (Translated by Roy A. Meals). 2006. Apr. P. 445.
12. Scheker L. R., Ahmed O. //Radical debridement, free flap coverage and immediate reconstruction of the upper extremity //Hand Clin. 2007; 23 P. 23–24.
13. Shihalëva NG, Chirkov IV //Treatment of patients with closed fractures of the distal metacarpals metaepiphysis using transosseous osteosynthesis. //The genius of orthopedics 2009 № 2. P. 40–45.

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Epidemiological and etiological aspects of genesis of periampullary tumors

Abstract: Purpose: Statistical data of tumors of a periampullary zone are presented in article. Among tumors of this localization the head of the pancreas (62–69.7%) is surprised most. Among the etiologic factors smoking can be taken for granted the factor twice increasing risk of a disease. The share of hereditary factors and the germinogen of mutations is found in 5–10% of patients. Direct influence of consumption of coffee and alcohol isn't considered

proved, and the previous diseases as pancreatitis and diabetes, make only a small contribution (4%) to risk of development of this heavy illness.

Keywords: periampullary tumors, epidemiology, prevalence, incidence frequency, mortality.

Periampullary tumors (PAT) in the last decade has become the leading cancer in the most industrialized countries, including Uzbekistan [1; 6].

Thus, according to Dolgushin B.I. (2008), Patyutko Y.I. (2013) PAT is 15% of all malignant neoplasms of the gastrointestinal tract, and tends to increase [35; 36; 45], and in the past 30 years the mortality has increased by 10–12 [4; 60; 69].

More than ten thousand people die from this disease in Western Europe every year, the same pattern is observed in Japan [22; 55; 56].

Among PAT tumors of the pancreatic head have the most incidence and explicit 62–69.7% of tumors of the periampullary zone (PAZ). Cancer of major duodenal papilla rank as the second incident and found in 12,7–30% cases, the cancer of the terminal part of choledoch observed in 12,8–15,1%. Duodenum have rare tumor affect5, accounting 2.4–3% of all the PAT [5; 13; 23].

The mean value rate of incidence pancreatic cancer (PC) in the world compound 10.4 per 100 thousand of population for males and 7.1 per 100 thousand in females [11; 34; 37], and the incidence of pancreatic cancer in the world is uneven. For example, among Afro-Americans the incidence is higher than in other population. Perhaps this is due to a genetic inability to inactivate carcinogens foods [2]. On the other hand, the fact of low incidence of pancreatic cancer in the African continent remains obscure. A possible answer to this phenomenon lies in the study of environmental factors. Overall, the incidence is higher in developed industrialized countries than in developing countries [62].

Among pancreatic localization over 60% of tumors are the tumors of the head. Cancer of the pancreatic head (CPH) often affects people of elder group, men 1.3–1.5 times more likely than women. The medial age of men compound 63.6 years and women — 66.5, according to by Siriwarden A.K. (2014) [54; 68].

According to the American Society of Surgeons, 37,170 of new CPH cases registered in 2013, with almost the same number among men and women (18830 and 18340 respectively) [25; 66; 67; 76].

In Japan and England, the rate of incidence in 2013 was 16 per 100 thousand of population [39], in Southern Europe this figure was 2.2 patients, in Asia-Pacific region — 6 patients, and in Nordic Europe — 11–12.5 cases per 100 thousand of population [42; 64].

The statistical data over the past years shows a steady increase in mortality from CPH, with 9th rank among all tumors, and 4th place among tumors of the gastrointestinal tract, and less in gastric cancer, colon and rectum [7; 26; 39]. Most sources devoted to the study of epidemiology of CPH highlights the sad fact is that almost equals the incidence of mortality. Such a ratio is not described for other tumors [9].

In the USA and Japan among the causes of death takes 4–5 of CPH place after lung cancer, colon cancer, breast cancer and prostate cancer [70; 73].

In Europe, as there is a high mortality rate: 10.8 for men and 5–7 women per 100 thousand of population [32]. In Russia from CPH every year die more than 13 thousand people, among the men attain 10 deaths per 100 thousand of population, ranking 6th among women, the figure 8.1 per 100 thousand of population, taking 8th place in the statistics of malignant neoplasms [3; 10; 34].

Cancer of the major duodenal papilla (cancer of Vater's papilla) in the structure of cancer incidence compound 0.5–3% of all malignant diseases of the gastrointestinal tract. Among PAT cancer of Vater's papilla found in 12.7–30% [19; 41; 49]. Morbidity with cancer of Vater's papilla compound 0.34 per 100 thousand of male population and 0.25 per 100 thousand of female population [63]. Cancer of Vater's papilla in men of working age are 2–3 times more often than women [65].

Cancer of the terminal part of choledoch (CTPCh) compound 2,8–4,6% of all malignancies and 15,3–16% of malignant tumors of PAZ [31]. According to foreign authors, the standardized incidence rate for cancer TPCh compound 0.67 per 100 thousand for men and 0.45 per 100 thousand for women [25; 30; 38]. According to Espinoza E., Hassani A., Vaishampayan U. (2014), the incidence of cancer of this localization of both men and women is the same [29]. There is no statistical data obtained for the TPCh cancer in Uzbekistan.

Primary **cancer of duodenum (CD)** is extremely rare (according to different authors — 0,6–6,1% of tumors of PAZ) and compound 0.3% of all tumors of gastrointestinal tract [8; 33; 52]. According to Edge S.B. (2010), Terada T (2012) CD comprise 0.04–0.5% of all the tumors of the gastrointestinal tract, 3.1% of intestine tumors and 25.4–50% of all tumors of the small intestine, equally frequent in men and women older than 50 years and almost not detectable at a young age [56].

It should be noted that the PAT is a cancer disease with severe course. Resectability often do not exceed 20%, hospital mortality among radical surgery 10–15%, and five-year survival rate — 25–30% [21].

Etiological background of development of the periampullary tumors. Genetic predisposition is one of the main causes of PAT [1; 7; 61]. PAT are more often in the elderly, in connection with the observed growth in frequency with the trend to increase the life expectancy in developed countries [18].

Thus, according to De La Cruz MS (2014), risk factors for CPH include the family history, smoking, chronic pancreatitis, obesity, diabetes, alcohol abuse, as well as possible dietary factors [25].

Moreover, some authors proved the correlation between endoscopic papillosphincterotomy (EPST) and development of CTPCh [14; 24; 57]. The reason for this is stasis and reflux of duodenal juice and pancreatic in the TPCh that possible lead to the formation of intestinal metaplasia of the epithelium and the development of adenocarcinoma [50; 72]. To confirm this Sharifiev S.Z. (2010) was described cases of carcinoid TPCh in patients after orthotopic liver transplantation for primary sclerosis cholangitis and multiple strictures of the bile ducts [12; 61].

Molecular and genetic studies carried out in the world prove different frequency of occurrence PAT depending on the population. Thus, patients in China are likely to have distinct expression of other K-ras and p53 genes [22; 27; 48]. Differences in the expression of these genes may be different survival rates and morbidity in Afro-Americans. In Japan, the mortality rate among men from CPH in 2012 was 1.7 times higher than in women [58]. These data may indicate that hormonal factors may be involved in the development and aggressiveness of CPH.

International Agency for Research on Cancer (IARC) has classified smoking cigarettes as a proven carcinogen pancreatic cancer (IARC, 1986). Under the auspices of IARC multicenter study using a case-control techniques in 5 regions of the world to illustrate the effect of smoking on the risk of pancreatic cancer [36]. This integrated study was conducted in centers in Australia, Canada, Netherlands and Poland. All centers used a common protocol and questionnaire and performed it so that it became possible to carry out a joint analysis. The study included 823 cases of smoking and 1,679 cases of population control. Cigarette consumption was established by a detailed questionnaire, which included all of the information about the frequency of smoking in each time period [62].

All centers showed a clear increase in the risk of disease of PAT depending on the number of cigarettes smoked and the pooled analysis of all data revealed statistically highly significant dose-dependent effect of smoking on the PAT. In the most severe smokers (more than 318 600 cigarettes in their lifetime), the relative risk was 2.7 (95% CI 1,95–3,74). These studies also showed that only smoking for 15 years or more increases the risk of cancer [44; 53; 74]. Extensive propaganda against smoking reduced the incidence of PAT in the USA population at the beginning of the 20th century.

Numerous association studies of diet and risk of PAT were indicated worldwide. Presumably, the 20% of the cases were associated with dietary factor. Presumably, the greater the total calorie intake, the higher is the risk of PAT. Increased nitrate content in food leads to the formation of nitrosamines. The use of vitamins and antioxidants should theoretically reduce the risk of cancer. However, the study [40; 59; 76] is not set a protective action of α -tocopherol and b-carotene on

the development of PAT for a 5–8-year period for the group observed. Also, do not set the relationship between folic acid and cancer of the pancreas. Possibly, a protective effect of vitamins and antioxidants significantly more evident with other types of malignancies and for longer use.

Endocrine system plays an important role in ensuring adequate immunological reactivity to tumor growth. A number of hormones is one of the most important parts of regulation of the immune reactivity of the organism and can cause both immunosuppression and stimulation of tumor tissue growth and its suppression. In modern experimental oncology no effective information models that reflect the maximum possible range of multidirectional interactions of the immune and endocrine systems in the dynamics of tumor growth.

However, most studies on the effects of vitamins and food consumption of fruit [46; 51; 74; 76], citrus fruits, vitamin C has a protective effect. Particularly interesting is the fact that natural citrus identified agents that are inhibitors of K-ras oncogene [15; 28].

Thus, the influence of dietary factors on the development of PAT attracts attention. It is known that the carcinogenic effects of many foods and eating habits may manifest themselves in several decades [75; 141].

The proportion of hereditary factors in the development of PAT is about 5–10% of all cases. To date, found that the gene BRCA2, one of the genes responsible for hereditary breast cancer is associated with the development and PAT and CPH. BRCA2 gene is considered to be a tumor suppressor, responsible for DNA repair. Mutation of this gene was found in both sporadic and hereditary CPH [20; 47].

Currently underway are numerous studies on genetic polymorphism on the development of cancer varying etiology. In particular, the role of the genes responsible for detoxification of carcinogens in products of smoking. The presence of an individual «favorable» genes may play a protective role. In this context, we investigated a genetic polymorphism of cytochrome P-450, N-acetyltransferases, glutathione-S-transferase, uridine-5-diphosphate glucuronyl. Noteworthy reports of the effect of acetylsalicylic acid and cyclooxygenase 2 in the risk of developing prostate cancer and PAT [16; 17; 43; 71].

Thus, speaking of Epidemiology of PAT, we can say the following: a clear correlation of risk factors and the development of PAT is found in certain parts of the diseased. Smoking can be considered proven factor doubles the risk of disease. The proportion of hereditary factors and germ cell mutation is found in 5–10% of patients. The direct influence of alcohol and coffee consumption is contested. Such prior diseases such as diabetes and pancreatitis, makes only a small contribution (4%) to the risk of PAT.

References:

1. Alimov A. V. Statistics on the activities of health care institutions of the Republic of Uzbekistan in 2013. – 2014. – 296 p.
2. Alexeytsev A. V. Features invasiveness of tumor growth of pancreatoduodenal zone, complicated by obstruction of bile duct//Creative surgery and onkology. – 2013. – № 1–2. – S.4–7.
3. Alibegov R. A., Sergeyev O. A., Narezkin D. V. et al. Optimization of processing methods of pancreatic stump during pancreatoduodenectomy//Surgery. – 2009. – № 9. – S. 41–45.
4. Burdyukov M. S., Nechipay A. M., Juric I. N., Chistyakov O. V., Romanenko N. V. Fine – needle puncture under the control of endoscopic ultrasonography in the diagnosis of tumors of biliopancreatoduodenal zone. Annals of Surgical Hepatology, 2010. – N 2. – S.66–71.
5. Kasatkin V. F. Ways to improve immediate results of pancreatoduodenectomy with periampullary tumors//Surgery. – 2008. – № 10. C. 10–16.
6. Kopchak V. M., Usenko A. Y., Chorny V. V. and others. Modern approaches in the surgical treatment of cancer of pancreatic head and organs of periampullary zone//Clinic surgery. – 2007. – № 2–3. – S.26–29.
7. Nazyrov F. G. Akbarov M. M., Saidazimov E. M. and others. Modern principles of diagnosis, surgical approach and techniques optimization of pancreatoduodenectomy in patients with periampullary tumors//Surgery of Uzbekistan. – 2013. – № 3. – S.52–53.
8. Nikulin M. P., Selcuk V. Y., Chistyakov S. S. Pancreatic cancer. Breast cancer. – 2012. – S.1726–1737.
9. Ogorodnik P. V. Deynichenko A. P. Endoscopic surgery of tumors of major duodenal papilla//Clinic surgery. – 2011. – № 4. – S.9–12.
10. Patyutko Y. I., Kudashkin N. E., Kotelnikov A. G., Abgaryan M. G. Gastropancreatoduodenal resection for malignant diseases complicated by mechanical jaundice. Surgery. Journal of them. N. I. Pirogov – 2011. – № 2. – S. 25–32.
11. Sidorov A. N., Zakharov A. G. Experience of surgical treatment of tumors of pancreas and periampullary zone//Bulletin ESSC SB RAMS. – 2012. – № 4. – S.90–92.
12. Chissov V. I., Starinskiy V. V., Petrova G. V.. State of cancer care in Russia population in 2011. M., 2012. 240 p.
13. Sharaf S. Z., Shaimardanov R. Sh., Kupkenov M. A. Prevention and treatment of suppurative cholangitis in patients with mechanical jaundice at high tumor block of bile ducts. Siberian Medical Journal (Tomsk). – 2010. – № 91 (2). – S. 243–245.
14. Shatveryan G. A. Pancreatoduodenal resection in the treatment of cancer of pancreatic head and periampullary zone: Author. dis. ... of M. D. – M., 2006. – 25 p.
15. Shchastny A. T., Petrov R. V., Egorov V. I. Results of dsauodenum preserve resection of pancreatic head by Beger during chronic pancreatitis. Annals of Surgical Hepatology. – 2011. – № 16 (1). S. 72–79.
16. Aichler M., Seiler C., Tost M., Siveke J., Mazur P. K., Da Silva – Buttkus P., Bartsch D. K., Langer P., Chiblak S., Dürr A., Höfler H., Klöppel G., Müller – Decker K., Briemeier M., Esposito I. Origin of pancreatic ductal adenocarcinoma from atypical flat lesions: a comparative study in transgenic mice and human tissues. J Pathol. 2012 Apr; 226 (5): 723–34.
17. Andres S. A., Wittliff J. L. Co – expression of genes with estrogen receptor – α and progesterone receptor in human breast carcinoma tissue. Horm Mol Biol Clin Investig. 2012 Dec; 12 (1):377–90.
18. Asuthkar S., Gondi C. S., Nalla A. K., Velpula K. K., Gorantla B., Rao J. S. Urokinase – type plasminogen activator receptor (uPAR) – mediated regulation of WNT/ β – catenin signaling is enhanced in irradiated medulloblastoma cells. J Biol Chem. 2012 Jun 8;287 (24): 20576–89.
19. Beger H. G., Poch B., Vasilescu C. Benign cystic neoplasm and endocrine tumors of the pancreas – when and how to operate – an overview. Int J Surg. 2014;12 (6): 606–14.
20. Björnsson E., Gustafsson J., Borkman J., Kilander A. Fate of patients with obstructive jaundice. J Hosp Med. 2008 Mar;3 (2): 117–23.
21. Carafa V, Nebbioso A, Altucci L. Sirtuins and disease: the road ahead. Front Pharmacol. 2012 Jan 31; 3–4.
22. Chandrabalan V. V., McMillan D. C., Carter R., Kinsella J., McKay C. J., Carter C. R., Dickson E. J. Pre – operative cardiopulmonary exercise testing predicts adverse post – operative events and non – progression to adjuvant therapy after major pancreatic surgery. HPB (Oxford). 2013 Feb 20.: 105–12.
23. Cho J. Y., Han H. S., Yoon Y. S., Hwang D. W., Jung K., Kim Y. K. Postoperative complications influence prognosis and recurrence patterns in periampullary cancer. World J Surg. 2013 Sep; 37 (9): 2234–41.
24. Corcione F., Pirozzi F., Cuccurullo D., Piccolboni D., Caracino V., Galante F., Cusano D., Sciuto A. Laparoscopic pancreaticoduodenectomy: experience of 22 cases. Surg Endosc. 2013 Jun; 27 (6):2131–6.
25. De Cecco C. N., Fina P., Fedeli S., David V. Role of magnetic resonance imaging in intrathoracic hepatocarcinoma diagnosis. Eur J Cardiothorac Surg. 2011 Feb; 39 (2):281.
26. De La Cruz M. S., Young A. P., Ruffin M. T. Diagnosis and management of pancreatic cancer. Am Fam Physician. 2014 Apr 15;89 (8): 626–32.

27. Delperio J.R., Bachellier P., Regenet N., Le Treut Y.P., Paye F., Carrere N., Sauvanet A., Autret A., Turrini O., Monges – Ranchin G., Boher J.M. Pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: a French multicentre prospective evaluation of resection margins in 150 evaluable specimens. *HPB (Oxford)*. 2014 Jan;16 (1): 20–3.
28. di Sebastiano P, Festa L, De Bonis A, Ciuffreda A, Valvano MR, Andriulli A, di Mola FF. A modified fast – track program for pancreatic surgery: a prospective single – center experience. *Langenbecks Arch Surg*. 2011 Mar; 396 (3): 345–51.
29. Eser S., Schnieke A., Schneider G., Saur D. Oncogenic KRAS signalling in pancreatic cancer. *Br J Cancer*. 2014 Aug 26;111 (5): 817–22.
30. Espinoza E., Hassani A., Vaishampayan U., Shi D., Pontes J.E., Weaver D.W. Surgical excision of duodenal/pancreatic metastatic renal cell carcinoma. *Front Oncol*. 2014 Aug 14; 4.
31. Fang Y., Shen K., Xue A., Ling J., Gao X., Shu P., Li H., Hou Y., Qin J., Sun Y., Qin X. Clinicopathological analysis of 80 patients with duodenum gastrointestinal stromal tumors. *Zhonghua Wei Chang Wai Ke Za Zhi*. 2015 Jan 25;18 (1):26–9.
32. Fathy O., Abdel – Wahab M., Elghwalby N., Sultan A., El – Ebidy G., Abu – Zeid M., Abd – Allah T., El – Shobary M., Fouad A., Kandeel T., Abo – Elenien A., El – Hah N.G., Abdel – Raouf A., Sultan A.M., Ezzat F. Surgical management of peri – ampullary tumors: a retrospective study. *Hepatogastroenterology*. 2008 Jul – Aug;55 (85): 1463–9.
33. Gall T.M, Jacob J., Frampton A.E., Krell J., Kyriakides C., Castellano L., Stebbing J., Jiao L.R. Reduced dissemination of circulating tumor cells with no – touch isolation surgical technique in patients with pancreatic cancer. *JAMA Surg*. 2014 May;149 (5): 482–5.
34. Goldner B., Stabile B.E. Duodenal adenocarcinoma: why the extreme rarity of duodenal bulb primary tumors? *Am Surg*. 2014 Oct; 80 (10): 956–9.
35. Grossjohann H.S., Rappeport E.D., Jensen C., Svendsen L.B., Hillingsø J.G., Hansen C.P., Nielsen M.B. Usefulness of contrast – enhanced transabdominal ultrasound for tumor classification and tumor staging in the pancreatic head. *Scand J Gastroenterol*. 2010 Aug; 45 (7–8): 917–24.
36. Gumbs A.A., Rodriguez Rivera A.M., Milone L., Hoffman J.P. Laparoscopic pancreatoduodenectomy: a review of 285 published cases. *Ann Surg Oncol*. 2011 May; 18 (5):1335–41. doi: 10.1245/s10434–010–1503–4.
37. Gundara J.S., Robinson B.G, Sidhu S.B. Evolution of the «autophagamiR». *Autophagy*. 2011 Dec;7 (12):1553–4. PMID:22024754.
38. Gurusamy K.S., Kumar S., Davidson B.R., Fusai G. Resection versus other treatments for locally advanced pancreatic cancer. *Cochrane Database Syst Rev*. 2014 Feb 27; 2: CD010244.
39. Hankiewicz – Ziolkowska K., Soboń M., Szyłberg T., Rudziński J. Duodenal bulb tumour of unknown origin. *Prz Gastroenterol*. 2014; 9 (6): 365–70.
40. Hirakawa T, Yashiro M, Murata A, Hirata K, Kimura K, Amano R, Yamada N, Nakata B, Hirakawa K. IGF-1 receptor and IGF binding protein-3 might predict prognosis of patients with resectable pancreatic cancer. *BMC Cancer*. 2013 Aug 21; 13: 392.
41. Hori Y.S., Kuno A., Hosoda R., Horio Y. Regulation of FOXOs and p53 by SIRT1 modulators under oxidative stress. *PLoS One*. 2013 Sep 11; 8 (9): e73875.
42. Ito K., Fujita N., Noda Y., Kobayashi G., Obana T., Horaguchi J., Koshita S., Kanno Y., Ogawa T., Kato Y., Yamashita Y. Impact of technical modification of endoscopic papillectomy for ampullary neoplasm on the occurrence of complications. *Dig Endosc*. 2012 Jan; 24 (1): 30–5.
43. Jemal A., Center M.M., DeSantis C., Ward E.M. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev*. 2010 Aug; 19 (8): 1893–907.
44. Kabashima – Niibe A., Higuchi H., Takaishi H., Masugi Y., Matsuzaki Y., Mabuchi Y., Funakoshi S., Adachi M., Hamamoto Y., Kawachi S., Aiura K., Kitagawa Y., Sakamoto M., Hibi T. Mesenchymal stem cells regulate epithelial – mesenchymal transition and tumor progression of pancreatic cancer cells. *Cancer Sci*. 2013 Feb; 104 (2): 157–64.
45. Kakisaka T., Kamiyama T., Yokoo H., Orimo T., Wakayama K., Tsuruga Y., Kamachi H., Hatanaka K., Taketomi A. Long – term survival of a patient with metachronous lymph node metastasis and bile duct tumor thrombus due to hepatocellular carcinoma successfully treated with repeated surgery. *Gan To Kagaku Ryoho*. 2013 Nov; 40 (12): 1831–3.
46. Kaplan M., Mahon S. Hot flash management: update of the evidence for patients with cancer. *Clin J Oncol Nurs*. 2014 Dec;18 Suppl: 59–67.
47. Kauppinen A., Suuronen T., Ojala J., Kaarniranta K., Salminen A. Antagonistic crosstalk between NF – κ B and SIRT1 in the regulation of inflammation and metabolic disorders. *Cell Signal*. 2013 Oct; 25 (10): 1939–48.
48. Kong S.L., Li G., Loh S.L., Sung W.K., Liu E.T. Cellular reprogramming by the conjoint action of ER α , FOXA1, and GATA3 to a ligand – inducible growth state. *Mol Syst Biol*. 2011 Aug 30; 7: 526.
49. Lassen K. Systematic review of five feeding routes after pancreatoduodenectomy. *Br.J. Surg*. 2013 Apr; 100 (5): 599.
50. Miyakawa S., Ishihara S., Horiguchi A., Takada T., Miyazaki M., Nagakawa T. Biliary tract cancer treatment: 5,584 results from the Biliary Tract Cancer Statistics Registry from 1998 to 2004 in Japan. *J Hepatobiliary Pancreat Surg*. 2009;16 (1): 1–7.

51. Miyazaki M., Kimura F., Shimizu H., Yoshidome H., Otuka M., Kato A., Yoshitomi H., Furukawa K., Takeuchi D., Takayashiki T., Suda K., Takano S. One hundred seven consecutive surgical resections for hilar cholangiocarcinoma of Bismuth types II, III, IV between 2001 and 2008. *J Hepatobiliary Pancreat Sci.* 2010 Jul; 17 (4): 470–5.
52. Mouchiroud L., Houtkooper R. H., Auwerx J. NAD metabolism: a therapeutic target for age – related metabolic disease. *Crit Rev Biochem Mol Biol.* 2013 Jul – Aug; 48 (4): 397–408.
53. North J. H., Pack M. S. Malignant tumors of the small intestine: a review of 144 cases. *Am. Surg* 2010; 66: 46–51.
54. Oberg K. E., Reubi J. C., Kwekkeboom D. J., Krenning E. P. Role of somatostatins in gastroenteropancreatic neuroendocrine tumor development and therapy. *Gastroenterology.* 2010 Sep; 139 (3): 742–53, 753.
55. Oguro S., Shimada K., Ino Y., Esaki M., Nara S., Kishi Y., Kosuge T., Kanai Y., Hiraoka N. Pancreatic intraglandular metastasis predicts poorer outcome in postoperative patients with pancreatic ductal carcinoma. *Am J Surg Pathol.* 2013 Jul; 37 (7): 1030–8.
56. Oguro S., Shimada K., Kishi Y., Nara S., Esaki M., Kosuge T. Perioperative and long – term outcomes after pancreaticoduodenectomy in elderly patients 80 years of age and older. *Langenbecks Arch Surg.* 2013 Apr; 398 (4): 531–8.
57. Ohtsubo K., Ishikawa D., Nanjo S., Takeuchi S., Yamada T., Mouri H., Yamashita K., Yasumoto K., Gabata T., Matsui O., Ikeda H., Takamatsu Y., Iwakami S., Yano S. Synchronous triple cancers of the pancreas, stomach, and cecum treated with S-1 followed by pancrelipase treatment of pancreatic exocrine insufficiency. *JOP.* 2013 Sep 10; 14 (5): 515–2.
58. Pottakkat B., Kapoor A., Prakash A., Singh R. K., Behari A., Kumar A., Kapoor V. K., Saxena R. Evaluation of a prospective surgical strategy of extended resection to achieve R0 status in gall bladder cancer. *J Gastrointest Cancer.* 2013 Mar; 44 (1): 33–40.
59. Qiu Y. D., Bai J. L., Xu F. G., Ding Y. T. Effect of preoperative biliary drainage on malignant obstructive jaundice: a meta – analysis. *World J. Gastroenterol.* 2011 Jan 21; 17 (3): 391–6.
60. Rees J. R., Macefield R. C., Blencowe N. S., Alderson D., Finch – Jones M. D., Blazeby J. M. A prospective study of patient reported outcomes in pancreatic and peri – ampullary malignancy. *World J Surg.* 2013 Oct; 37 (10): 2443–53.
61. Rosso E., Langella S., Addeo P., Nobili C., Oussoultzoglou E., Jaeck D., Bachellier P. A safe technique for radical antegrade modular pancreatosplenectomy with venous resection for pancreatic cancer. *J Am Coll Surg.* 2013 Nov; 217 (5): e35–9. doi: 10.1016.
62. Sannappa R. M., Buragohain J., Sarma D., Saikia U. K., Choudhury B. K. Agenesis of dorsal pancreas associated with periampullary pancreaticobiliary type adenocarcinoma. *JOP.* 2014 Sep 28; 15 (5): 489–92.
63. Schiffman S. C., Nowacki M. R., Spencer L., McMasters K. M., Scoggins C. R., Martin R. C. Molecular factors associated with recurrence and survival following hepatectomy in patients with intrahepatic cholangiocarcinoma: a guide to adjuvant clinical trials. *J Surg Oncol.* 2014 Feb; 109 (2): 98–103.
64. Shikano T., Nakao A., Kodera Y., Yamada S., Fujii T., Sugimoto H., Kanazumi N., Nomoto S., Takeda S. Middle pancreatectomy: safety and long – term results. *Surgery.* 2010 Jan; 147 (1): 21–9.
65. Shonaka T., Inagaki M., Akabane H., Yanagida N., Shomura H., Yanagawa N., Oikawa K., Nakano S. Total pancreatectomy for metachronous mixed acinar – ductal carcinoma in a remnant pancreas. *World J Gastroenterol.* 2014 Sep 7; 20 (33): 11904–9.
66. Shukla P. J., Barreto G., Shrikhande S. V. The evolution of pancreatoduodenectomy. *Hepatogastroenterology.* 2011 Jul – Aug; 58 (109): 1409–12.
67. Sikkens E. C., Cahen D. L., de Wit J., Looman C. W., van Eijck C., Bruno M. J. A prospective assessment of the natural course of the exocrine pancreatic function in patients with a pancreatic head tumor. *J Clin Gastroenterol.* 2014 May – Jun; 48 (5): 43–6.
68. Sikkens E. C., Cahen D. L., de Wit J., Looman C. W., van Eijck C., Bruno M. J. Prospective assessment of the influence of pancreatic cancer resection on exocrine pancreatic function. *Br J Surg.* 2014 Jan; 101 (2): 109–13.
69. Siriwardena A. K., Siriwardena A. M. Pancreatic cancer. *BMJ.* 2014. Oct 31; 349.
70. Somani A., Jain A. K., Dixit V. K. Periampullary carcinoid: an uncommon tumor at an unusual site. *Indian J Cancer.* 2011 Oct – Dec; 48 (4): 496–9.
71. Sugawara A., Kunieda E. Effect of adjuvant radiotherapy on survival in resected pancreatic cancer: a propensity score surveillance, epidemiology, and end results database analysis. *J Surg Oncol.* 2014 Dec; 110 (8): 960–6.
72. Takahashi R. U., Makiko O., Ochiya T. Role of microRNA in cancer development: biology and clinical applications. *Nihon Geka Gakkai Zasshi.* 2012 Mar; 113 (2): 197–203.
73. Takami K., Moriya T., Kamiga T., Abe T., Miseki T., Oku T., Aoki Y., Tominaga T. Adenocarcinoma of the minor duodenal papilla: report of a case. *Case Rep Gastroenterol.* 2011 Apr 13; 5 (1): 172–8.
74. Tani M., Kawai M., Hirono S., Okada K. I., Miyazawa M., Shimizu A., Kitahata Y., Yamaue H. Randomized clinical trial of isolated Roux – en – Y versus conventional reconstruction after pancreaticoduodenectomy. *Br J Surg.* 2014 Aug; 101 (9): 1084–91.
75. Van Stijn M. F., Vermeulen M. A., Siroen M. P., Wong L. N., Van den Tol M. P., Ligthart – Melis G. C., Houdijk A. P., Van Leeuwen P. A. Human taurine metabolism: fluxes and fractional extraction rates of the gut, liver, and kidneys. *Metabolism.* 2012 Jul; 61 (7): 1036–40.

76. Wang X., Ouyang Y., Liu J., Zhu M., Zhao G., Bao W., Hu F. B. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose – response meta – analysis of prospective cohort studies. *BMJ*. 2014 Jul 29; 349.

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Clinical characteristics and principles of treatment of patients with enteric infections caused by clostridium difficile

Abstract: The risk factors and the development of diarrheal and intoxication syndrome in patients with intestinal infections caused by *Clostridium difficile* is an early irrational use of antibiotics, prolonged hospital stay as a source of nosocomial infections, as well as age.

Keywords: Intestinal infections, intoxication syndrome, diarrhea.

At the present stage the problem of microbial ecology associated with the effect of antibiotics on individual normal microflora of the human body is quite acute. With violation of the microecology due to extensive and occasionally unreasonable use of antibiotics is associated widespread caused by *Clostridium difficile*, clinical spectrum of symptoms that varies widely — from the carrier state and the very short-term passing of diarrhea until development of pseudomembranous colitis [1; 2; 5].

It was found that the toxins produced by these bacteria are involved in the pathogenesis of antibiotic-associated diarrhea and is currently considered as the most probable cause of colitis and diarrhea in children. All patients with diarrhea associated with antibiotics flowing with intoxication and leukocytosis, the occurrence of acute diarrhea should be associated with *C. difficile*. In samples of stool *C. difficile* cells remain viable at 5 °C to 10 days at 25 °C up to 4 days.

One of the features of *C. difficile* is the production of heat labile complex exotoxin consisting of a cytotoxin (toxin B) and enterotoxin (toxin A) with said complex binds toxic pathological changes in intestinal mucosa of the patient: ulcer formation and false-membranous colitis.

Clostridium difficile causes of pseudomembranous colitis in 100% of cases. *Clostridium difficile* intestinal infection occurs in approximately 50% of newborns. A pathogenic property of the pathogen does not occur until the end of the first year of life due to lack of or underdeveloped intestinal receptors for the toxins produced by them. At the same time, asymptomatic carriage of *Clostridium difficile* detected in a certain part of the adult population — 1–3% in Europe and 15% in Japan. In our country, a number of reasons, and primarily due to the lack of appropriate laboratory facilities, diagnosis of infections caused by *Clostridium difficile* is absent and its frequency may be judged only on the basis of individual publications.

Purposes. The purpose is study of clinical features of intestinal infections in children caused by *Clostridium difficile*.

Materials and methods. Our systematic study of the etiology of acute intestinal infections in children for the period of 2005–2012 years based on studies of 225 sick children aged 2 months to 3 years. The material for the study were samples of faeces. The study was conducted using the polymerase chain reaction (PCR) and bacteriological methods. Diagnosis by PCR analysis was installed in all cases. Of these, 14 (38.8%) children were diagnosed on the basis of bacteriological tests and 32 (88.8%) children on the basis of serological (ELISA).

The criteria for assessment of the severity of the disease were: the acuteness of infection, the severity of toxicity and exsiccosis, duration of temperature reaction and gastrointestinal disorders, the degree of involvement in the pathological process of the cardiovascular and central nervous system, blood counts and coprogram. Given these criteria of 36 examined patients were diagnosed with moderate form in 24 (76.6%) and heavy in 12 (33.4%).

To determine the causative agents of acute intestinal infection in this work first time we have used PCR.

Observed patients before admission to hospital had been treated with antibiotics, bacterial preparations received on the set in the history of various degrees and kinds of intestinal dysbiosis. These children have been carried out paraclinical methods of examination, including the study of intestinal microflora.

Results and discussion.

According to the results of research *Clostridium difficile* is found in 16% of cases of children with acute intestinal infections. The average age of patients caused by *Clostridium difficile* was $13,7 \pm 1,35$. Thus, in the age group 1–2 years among identified an acute intestinal infection predominated clostridial diarrhea. In this group of patients *Clostridium difficile* is the leading causative agent of an acute intestinal infection causing about half of all diagnosed cases of etiologically undiagnosed intestinal infections.

Our results showed that the infection is significantly more common in children younger than 2 years ($P > 0,05$) (Table 1).