Results. In type 1 VWD mutations are located throughout the VWF gene from the promoter region to exon 52 and the majority are missense mutations (75%), whereas splice, deletion, nonsense, insertion, duplication, and large in-frame deletions mutations comprise minor proportions. The most common locations for mutations in type 2A WVD are: the A2 domain (p.Arg1315Cys, p.Arg1374Cys and p.Arg1374His) , D3 domain (missense mutations are located in ex22 and 25 to 28, many introducing/substituting cysteine residues; replacement of p.Cys1130 is the most common change), D2 domain (mutations are recessively inherited and are located in ex11 to 16), and CK domains (mutations affect ex51 to 52). Mutations in type 2B and 2M are located in the A1 domain (ex 28). Type 2N VWD is caused by mutations in ex 17-20 and 24-25 (missense mutations or null allele). The most frequent mutation in the European populations is p.Arg854Gln, for which ~1% of individuals are heterozygous. In type 3 VWD the mutation location is 5′ VWF-Ex52 (missense mutations or null allele).
Conclusions. VWF mutations are located throughout the VWF gene, resulting in a wide range of mutation types that cause quantitative and qualitative disorders. VWF protein is involved in several processes that can be damaged by mutation, and the varying phenotypes in VWD illustrate the processes that are impaired.
Key words: von Willebrand disease (VWD), mutation, bleeding disorder

321. GENETIC PREDISPOSITION IN GASTRIC CANCER

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Introduction. Gastric cancer is a neoplasm with a starting point in the gastric mucosa, representing one of the most common malignant visceral locations. Although a decreasing incidence globally, gastric cancer remains one of the most common causes of cancer death. Diagnosed in the early stage, it is curable, but unfortunately, most cases are identified late, in advanced stages.
Aim of the study. Elucidation of predisposing factors and molecular mechanisms underlying gastric cancer development.
Materials and methods. Exploring bibliographic sources using databases: PubMed, Google Scholar
Results. Gastric cancer presents a multifactorial pathology caused by the interaction between environmental factors - *Helicobacter Pylori*, major cancer agent - and the genetic factors of the host organism. Genetic predisposition plays a major role in gastric carcinogenesis, as there are classes of genes involved in mucosal protection, immune response to *H. pylori* infection, carcinogen detoxification, antioxidant protection, DNA damage repair and ability to cell proliferation. The protective genes of the gastric mucosa are the mucin genes. The subtypes MUC1 (G allele at rs4072037), MUC2, MUC5AC, MUC6 and the genes of the trefoil peptide-pS2 peptide, factor 1 (TFF1), spasmolytic polypeptide (SP) and intestinal ITF factor). Detoxification genes: cytochrome P450 (CYP450) linked to metabolism I-CYP1A1 (Ile462Val), CYP2E1 and CYP2C19. Glutathione S-transferases (GSTs) in Phase II play a role in protecting cells against the onslaught of chemical carcinogens. The pro and anti-inflammatory genes IL1B, TNF, LTA, IL 6, IL1RN, IL 10 and TGF B, play a key role in the development of CG.DNA-repair genes include methylenetetrahydrofolate reductase (MTHFR-

C677T mutation, XRCC1 gene (Arg194Trp), HOGG1 with TT genotype, xeroderma pigmentosum (XPF) (rs744154) increase susceptibility. Tumor suppressor genes: p53 (Arg / Arg), p53CD72 associated with genetic susceptibility to gastric cancer is an important biomarker. *H. pylori* infection and p53 mutation have been shown to have a synergistic effect. NM23 is the first confirmed suppressor gene for tumor metastases.

Conclusions. The study is based on the analysis of genetic variants that confer a higher risk of CG and their interactions with environmental factors, respectively *H. pylori* infection. Candidate gene polymorphisms in gastric cancer susceptibility. A deeper understanding of the factors involved in the development and progression of CG may allow the identification of persons at risk and can provide useful predictive information for the subgroups of patients who need early treatment or surveillance strategies.

Key words: Gastric cancer, genetic predisposition.

322. THE GENETIC PARTICULARITIES IN PAPILLARY THYROID CANCER

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Introduction. Papillary Thyroid Cancer (PTC) is taking the 1st place in malign processes of endocrine system, being also the most studied problem in cases of thyroid gland cancer. PTC is taking 40-85% from the total of the thyroid cancer in the past few decades. This is because of the human activity in the past- pollution of the environment, the rise of the radioactivity in the water, air and ground, registered a sudden rise in morbidity in EU and USA. We would like to mention the genetic factor in etiology of PTC. It has been recently shown that these tumors commonly have one of three genetic alterations: BRAF point mutations, RET/PTC rearrangements, or RAS point mutations. This factor has to have a substantial role in precocious diagnosis of the cancer and prognosis after the chirurgical treatment.

Aim of the study. To elucidate the role of the genetic modifications in pathogenesis and cancerogenesis of the disease

Materials and methods. We performed a retrospective study on a group of 50 patients with thyroid cancer, who were investigated: clinical, ultrasound, histological and laboratory (thyroid hormone level) and treated in the oncological "Head and neck" department of the Institute of Oncology between December 15- May 30, 2019 . The study included primarily diagnosed cases with CPT after surgical intervention. Data on the main risk factors, demography and tumor location have been collected from medical records. We will classify the patients after age, sex, cancer stage, evolution rate, data about the family anamnesis: the presence if the thyroid nodular disease and the presence of another neoplastic processes in relatives.

Results. 83% of patients were diagnosed with CPT, 80% are female, middle age of involvement of 51-60 years old (38%). We observe hypoplasia of the thyroid gland on 6 patients (12%); hyperplasia of grade l-ll on 27 patients (54%); hyperplasia of grade lll-lV on 16 patients (33%). According to hormonal levels, euthyroidism, had 18 patients (37%); hypothyroidism 10 patients (21%); hypothyroidism 21 patients (42%). CPT patients were diagnosed in pTNM following stages: st.l T1N0M0, 7 patients (15%); st.ll T2N0M0, 22 patients (45%); st.lll T3N1M0, 15 patients (30%); st.lV T4N1M1, 5 patients (10%). From the studied group, 19 patients have relatives with nodular pathology of the thyroid gland (37%).