Materials and methods. A group of 46 infertile men were investigated during genetic counseling among infertile couples referred for ART treatment. Criteria for including patients were fulfilled if they presented with oligo/azoospermia, raised or normal levels of FSH, LH and testosterone. Genomic DNA was isolated and used to analyze AZF microdeletions by PCR. The regions and sequence-tagged sites of AZFa (SY86, SY84), AZFb (SY127, SY134), and AZFc (SY254, SY255) were sequenced by multiplex PCR. Five non-obstructive azoospermic men had Y chromosomal microdeletions. All five Y-microdeleted men underwent microsurgical observation of testicular architecture and quantitative histology of spermatogenesis in a strip of testicular tissue. The results were compared with the different type of Y microdeletion.
Results. Deletions of Y chromosome were seen in the AZFc regions of 2 patients, deleted markers were sY254 and sY255. In both men with AZFc deletions, the histological defects were variable, but no sperm were found. In only one case the defect of Sertoli cell-only syndrome (SCOS) in patient with microdeletions in each region of AZFa-sY84, sY86; AZFb-sY127, sY134; AZFc-sY254, sY255 was present. One patient with deletion of AZFb (SY127, SY134) had spermatogenetic maturation arrest. In all men with AZF microdeletions of the Y chromosome, we found severe spermatogenic defects: however, we also did not find, in all of them, mature sperm sufficient for ICSI. The patients were advised to use sperm from the donor for ICSI and IVF.
Conclusions. This study highlights for all couples with the diagnosis of male infertility with oligo/azoospermia the need of genetic testing and counseling prior to employment of assisted reproduction techniques. This is important for providing a firm diagnosis and fertility treatment to couples with infertility and for prevention of the transmission of AZFc deletions through ICSI to offspring.
Key words: male infertility, PCR, deletion, AZF region

320. GENETIC ASPECTS OF VON WILLEBRAND DISEASE

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Introduction. Von Willebrand disease (VWD), the most common inherited bleeding disorder in humans, is a heterogeneous disorder caused by a partial quantitative (type 1 VWD), qualitative (type 2 VWD) or severe quantitative (type 3 VWD) deficiency of von Willebrand factor protein (VWF). It is characterised clinically by mucocutaneous bleeding, such as epistaxis and menorrhagia, and prolonged bleeding after surgery or trauma. VWF is a large, multimeric protein that plays a role in platelet adhesion and serves as a carrier for the thrombotic protein factor VIII. The VWF gene is located at the short arm of chromosome 12 (12p13.31). Depending on its type, VWD can either have an autosomal dominant inheritance pattern (type 1, type 2A, 2B, 2M) or an autosomal recessive inheritance pattern (type 2N and type 3).
Aim of the study. Expanding the understanding of the genetic basis of different types of VWD.
Materials and methods. This study is based on a review of different articles from the open access data bases: PubMed, OMIM, SpringerLink.

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-