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**Abstr**

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S83**

***PS-03-028***

***Morphological base of pelvic pain syndrome in deep endometriosis***

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**Objective:** Endometriosis (EM), which is an abnormal appearance of endometrial tissue outside of uterus, has chronic pelvic pain as one of the corec linical manifestation san dposes a major challenge for the health care system. Aim of the study: to examine morphology and neural tissue markers in endometriosis lesions of various anatomic localisations in women with and without pain syndrome.

**Method:** We studied surgical samples (colon, urinary bladder, rectovaginal septum, peritoneum of the lower pelvis) from 52 patients diagnosed with either «pain-free» variant of EM (cohort #1) or EM accompanied with pain syndrome (cohort #2). Tissue sections from paraffin-embedded samples were subjected to immunohistochemistry via standard protocols with the following pri- mary antibodies: PGP 9.5; NF (clone 2 F1); NGF (clone E-12); NGFRp-75 (all – from Dako, Denmark).

**Results:** chronic inflammation, per neural type of growth, neuromas de- velopment in foci of EM and remodeling of nerve fibers and neural endings in endometriosis lesions, with PGP 9.5, NGF and NGFRp-75 involved in formation of new nerve fibers result in formation of chronic pain syndrome in EM. **Conclusion:** Morphological characteristics and immunohistochemical phenotype of EM lesions was independent of their anatomic localisation but showed good correlation with pain status of the patients.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S84**

***PS-03-035***

***Molecular mechanisms and morphology of leiomyoma reduction in- duced by selective progesterone receptors modulators***

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**Objective:** To study molecular mechanisms and morphological substrate of leiomyoma reduction in reproductive-age patients, receiving a selective progesterone receptor modulator (SPRM) for 3 months.

**Method:** The study was performed on leiomyoma taken during laparoscopic myomectomy from 75 reproductive-age women with uterine myoma, accompanied by menorrhagia and anemia. 40 patients underwent surgery after 3 month SRPM treatment (group I) and 35 patients underwent surgeryonly (groupII). Morphological and immunohistochemical analysis (SRC-1, NCoR-1, ER, PgR, Ki-67, p16, TGF-β, VEGF) were made.

**Results:** In group I excessive bleeding stopped after 4–7 days from start of treatment, ultrasound revealed decrease in fibroid size (p < 0,05), Hb level increased (p < 0,01). The morphological substrate of leiomyoma reduction in I group were apoptosis and dystrophic changes of leiomyocytes, sclerosis and hyalinosis oftumour stroma and vesselwalls sclerosis, with low ki-67 and p16 increase, low VEGF and TGF-β and hormonalreceptiondysregulationrevealedinlowSRC-1expressionwith unchanged levels of NCoR-1, ER, PR.

**Conclusion:** Molecular mechanisms of tumour reduction included SRC- 1,Ki-67, VEGFandTGF-βdecreaseandp16increase insmoothmuscle cells, with unchanged levels of PR, ER and NCoR-1. Obtained results show increase in apoptosis, decrease in proliferation and angiogenesis as a morphological base of leiomyoma reduction.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S85**

**S-03-040**

***Mechanisms of development of large leiomyomas***

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**Objective:** Large leiomyomas (LL) of the uterus are characterized by increasing of the uterus due to myomatous nodes up to the size of a 12 week pregnancy and more. The aim was tostudy mechanisms of LL development based on immunohistochemical (IHC) studies of Ki67, TGFβ, CD117, PD-ECGF, connexin and nestin.

**Method:** biopsy and postoperative material of 54 patients with simple tipe leiomyomas wereanalized. Patients weredividedinto two groups with LL and control with leiomyomas, less than 4 cm in diameter. Each group was divided into two subgroups by age: women younger than 45 years and women over 45 years. Immunohistochemistry (IHC) determined the ex- pression of Ki67, TGFβ, CD117, PD-ECGF, connexin and nestin.

**Results:** IHC showed increased expression of Ki-67, PD-ECGF, TGFβ in growth zones in LL in comparison with small leiomyomas, especially in women over 45 years of age.

**Conclusion:** Pathogenetic mechanisms of growth of LL are associated withactivation of stem and progenitor cells in the perivascular regions of LL growth, which is manifested in the enhancement of expression of the stem markers TGFβ, CD117, PD-ECGF, Ki67, connexin and nestin in the cell sof the irgenera. The mostpronouncedactivityofgrowthzonesby molecular markers is found in women with leiomyomas larger than 45 years, which requires oncological alertness.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S87**

**PS-03-046**

**Molecular features of uterus leiomyoma in reproductive-age women after previously performed inefficient Uterine Artery Embolisation (UAE), focused ultrasound ablation controlled by MRI (MRgFUS) and myomectomy**

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**Objective:** to investigate the morphological, immunohistochemical fea- tures of uterus leiomyoma in reproductive-age women after previously performed UAE, MRgFUS ablation of fibroids and myomectomy.

**Method:** The study was performed on leiomyoma taken from 110 wom- en36,2±5,2years.GroupI(n=32)-patientswithhistoryofUAE,group II (n = 26) - patients after MRgFUS ablation and group III (n = 52) - patients, after myomectomy. The study included patients with ineffective treatment of fibroids. morphological and immunohistochemical investgation (VEGF, HIF-1, IGFR-1, Casp3, Ki67) was made. **Results:** VEGF was high in group III, lower in group I and the lowest in groupII.HIF-1 wassignificantlyhigheringroupI (10.1%) wasmoderate in group III (5.0%); and itwasverylowinthegroupII (0.26%),thatwas statistically significant, p < 0.05. In Group I, IGFR was 1.5 points; in group II-3,6 points; in group III - 2.7 points, p < 0.05. Ki 67 and Casp3 were low and comparable in all groups.

 **Conclusion:** Obtained results show that in spite of different mechanisms of leiomyoma growth after inefficient initial treatment (UAE induces HIF-1 expression, MRg FUS may trigger growth through IGFR) the mechanisms of cell cycle regulation are preserved in all groups.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S87**

**PS-03-047**

***The syndrome of undifferentiated Connective Tissue Dysplasia (uCTD) in a combination with Hereditary Thrombophilia (HT) as a cause of primary female infertility***

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**Objective:** ThecombinationofsyndromeofuCTDandHToftenac company female infertility. The purpose was to study morphological and immunophenotypic features of the endometrium in patients with primary infertility in uCTD and HT.

**Method:** The study was performed on endometrial pipelle-biopsies taken in the“implantation window” from 81 patients with clinical diagnosis of uCTD (13 women), HT (40), with combination of uCTD and HT (19) and control group - healthy surrogate mothers (9). Morphological and histochemical study (hematoxylin and eo- sin, pikrofuksin by Van Gieson, toluidine blue) and immunohistochemical study with the antibodies to ER, PgR, LIF, PAI-1, VEGF, collagen I, collagen III, fibronectin, laminin, MMP-2, MMP-9 were performed on endometrial biopsy specimens.

**Results:** Main groups (uCTD, HT, uCTD + HT) showed signs of impaired endometrial receptivity: decrease of mature pinopodes level, retarding endometrial maturation, decrease of LIF, VEGF, and stromal progesterone and estrogen receptors expression and PAI-1 increase, compared to control. Foci of sclerosisinendometrialstromainpatientofmaingroupsshowedaccumulation of collagen III, MMP2 and 9, fibronectin and laminin.

**Conclusion:** Obtained results show impaired endometrial receptivity in patients with uCTD, HTand especially with combination of these condi- tions. Endometrial stroma undergoes remodeling ending in stromal focal sclerosis, reduced endometrial receptivity and infertility.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S96**

**PS-03-095**

***Endometrial receptivity in patients with Uterine Myoma (UM) after previously performed ineffective Uterine Artery Embolisation (UAE),FocusedUltrasoundAblation(FUA)andMyomectomy(ME)***

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**Objective:** The aim of the study was to endometrial receptivity in reproductive-age women suffering from UM after ineffective UAE, FUA and ME.

**Method:** The study was made on pipelle-biopsies of endometrium taken from 39 reproductive-age women (36,2 ± 5,2 years) suffer- ing from UM after ineffective UAE (13), FUA (13) and ME (13) in secretory phase after ineffective treatment (group A) and 3 months later after repeated ME (group B). Histological and immunohistochemical (IHC) examination was performed with pri- mary antibodies to PgR, ER and LIF.

**Results:** Morphological analysis of endometrium showed retarding endometrial maturation, decrease in pinopodes level, decrease in PgR, ER and LIF in group A, these characteristics were improved in group B. The worst ER and PgR and the lowest LIF were in patients after FUA, a little better in patients after UAE. In pa- tients with ME stromal PgR/ER index was the best in groups A (1,91) and B (1,98) and LIF expression was higher (1,9 and 3,8, respectively).

**Conclusion:** Obtained results show better endometrial receptivity after inefficient ME, compared to UAE an FUA, with the worst parameters in the latter group. Nevertheless, all patients show improve of endometrial implantation potential in 3 months after repeated myomectomy supporting the idea of reversibility of these changes.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S108**

***PS-05-027***

***Pulmonary lesions with bone marrow, bone trabeculae and calcium deposition:Possibleinvolvementofbonemarrowmesenchymalstem cells in repair of lung tissue in pathological conditions***

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**Objective:** to study morphology and molecular mechanisms of develop- ment of pulmonary lesions with bone marrow, bone trabeculae and cal- cium deposition.

 **Method:** surgical material from patients with healed foci of pri- mary tuberculosis (4 patients) and nontuberculosis mycobacteriosis (1 patient) and autopsy case of patient with candidiasis after chemotherapy and colon cancer progression (1 case). Imunnohistochemistry (IHC) analysis of Apo-Cas, Ki67, SMA, Desmin, Vimentin, CD3,20,45,68, EMA, TGF-β, CD34, PDGF, OCT-4, CD117 was done.

**Results:** Healed foci of primary tuberculosis were solitary and localized in 3, 6 and 7 segments of the lungs, characterized by dystrophic calcifi- cation of central caseous necrosis surrounded by fibrous capsule around with foci of bone trabeculae and bone marrow. In other patient with diffuse pulmonary osteodystrophy lesions were multiple and characherized byformationofboneswithbonemarrowandcalcification. IHC of these lesions showed stem cells with expression of Ki67, SMA, Desmin, Vimentin, CD3,20,45,68, EMA, TGF-β, CD34, PDGF, OCT-4, CD 117.

**Conclusion:** Lesionswithbonemarrow,bonetrabeculaeandpresence of stemcellsmayprovetheinvolvementofbonemarrowmesenchimalstem cells in repair of lung tissue in pathological conditions.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S116-117**

***PS-06-023***

***Impact of insulin resistance on epidermal growth factor receptors in patients with seborrheic keratosis A. Aleksandrova\*, V. Smolyannikova, V. Filatova, E. Ryaboshtanova \*First Moskow State Med. University, Dept. of Pathological Anatomy, Russia***

***Objective:*** To examine epidermal growth factor receptors (EGFR) expression in patients with seborrheic keratosis (SK) and insulin resistance (type 2 diabetes mellitus) and in patients without con- comitant carbohydrate metabolism disorders.

**Method:** The study involved 80 patients with SK, 40 of them with concomitant type 2 diabetes mellitus. The immunohistochemical test with monoclonal antibodies to EGFR (clone EGFR.25) has been performed.

**Results:** Intense diffuse staining of the tumour cells membranes has been identified in 32 patients with type 2 diabetes mellitus (80 %), moderate staining - in 6 patients (15 %) and weak— in 2 (5 %). A positive reaction was weak by patients without con- comitant carbohydrate metabolism disorders in 28 cases (70 %), moderate - in 8 patients (20 %) and pronounced - in 4 patients (10 %).

**Conclusion:** EGFR overexpression identified in patients with SK and concomitant type 2 diabetes mellitus has been conditioned by insulin resistance, wherein insulin signal transmission control failures in the cell result in changes in the EGF synthesis and signaling pathway, controlling cell proliferation and growth.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S122**

***PS-06-045***

 ***Experience of application immunofluorescence antigen mapping for morphologic diagnosis of different types of congenital epidermolysis bullosa***

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**Objective:** to optimize the morphological diagnosis of different types of CEB.

 **Method:** 28 skin biopsies from 14 patients with different types of CEB were investigated. The investigators performed histological examination of skin fragments taken from a bullous area and immunofluorescence antigen mapping using the indirect immunofluorescence test (IIFT) with antibodies against structural proteins of the dermal- epidermal junction (laminin α3, β3, and γ2 chains, keratins 5 and 14, types VII and XVII collagen, α6 andβ4 integrin subunits, desmoplakin, plectin, kindlin-1, and plakophillin) of the apparently unaffected skin.

**Results:** Immunofluorescence antigenmappingcould determine the type of CEB inallcasesandin 86% of casesidentifytheprotein, the impaired production of which was responsible for the development of the disease.

**Conclusion:** Immunofluorescence antigen mapping is an integral part of the comprehensive morphological diagnosis of CEB, acting as an inter- mediatebetweenthemorphologicalverification of CEB diagnosis and the targeted search for mutations by a molecular genetic method.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S168**

**PS-10-029**

***Structural-moleculardisordersofendometrialreceiptivityininfertile women, suffering from external genital endometriosis***

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**Objective:** Study of structural and molecular disorders in endometrial receptivity in infertile women with external genital endometriosis (EGE).

**Method:** Morphological and mRNA studiesof94womenwithEGE and infertility without combined genital pathology and 54 control woman were carried out. Immunohistochemically LIF, HOXA10, glycodelin A, integrinαv β3, estrogenan dprogesteronereceptors, aromatasewerestudied. mRNA of the LIFR, LIF, ESR1, PGR, HOXA10, and PTEN genes was determined by RT-PCR.

**Results:** Patients with EGE have following particularities: 2.4 times de- creaseinthe area occupiedbypinopodeson the surfaceepitheliumofthe endometrium, a lower expression of the LIF (4.2 + 0.7 and 5.7 + 0.3 points Respectively), HOXA10 (1.8 + 0.4 and 4.0 + 0.4 points), integrin αvβ3(0.7+0.4and2.4+0.4points), glycodel A (1.0+0.3and1.7+0.3 points) (p > 0.05), an imbalance in the expression of estrogen and progesterone receptors, an increase in aromatase expression (5.8 and 3.7 points), anda decrease in theexpressionofNOxA10 mRNA in1.4times (p>0.05),LIFin1.7times(p>0.05),progesteroneReceptorin1,6times (р > 0,05),РТЕN in 1,4 times ( р > 0,05). **Conclusion:** Infertility in endometriosis can be associated withstructural immaturity and molecular disorders in endometrium.

1. **Vircows Arch, 2017, 471 (Suppl.1), S290**

**PS-25-131**

***Varicocele in children - to operate or not to operate: That is the question***

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**Objective:** the question about necessity of children with early var- icocele grade operative treatment still is not answered. Our study was devoted to revealing the varicous vein wall compensatory ability.

**Method:** we investigated vein intraoperative biopsies from 28 children with different varicocele grades.Light microscopy with picrofuchsin and Weigert’s staining, immunohistochemistry were used. **Results:** in early varicocele grade in middle and small vein walls we found predominantly external longitudinally SMC hypertrophy with diffuse wall thickening, one-sided multiple tall fibromuscular pillows. Well-formed elastic carcass—wall arterialization was present in large veins. Prominent intermuscular sclerosis with SMC band “coupling” was detected in middle vein walls in III varicocele grade. Fibrosis severity gave positive correlation with TGFβ1 overexpression and negative—with α-SMА expression. **Conclusion:** compensatory vein wall remodeling was found in any diameter vein walls in early varicocele grade. We consider surgi- cal approach to be reasonable in II and III varicocele grade, when progressive fibrosis and varicous vein wall rigidity induce heavy hemodynamic disorders, prolonged hypoxia and testicular atrophy.

1. **Virchows Arch (2017) 471(Suppl 1):S1–S352 S336**

**E-PS-13-001**

**Morphometric characteristics of reparative, neoplastic and cancer spheroid epithelial-mesenchymal *structure in cervical biopsy***

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**Objective:** We evaluated the morphometric characteristics of reparative, neoplastic and cancer SEMS in biopsy with HPV associated uterine cer- vical cancerogenesis.

**Method:** Samples of 54 patients with uterine pathologies (15 chron- ic cervicitis, 12 L-SIL, 15 H-SIL and 12 carcinoma) were obtained and studied histological. Materials were fixed with 10 % formalin solution, parafinized then microtomed horizontally to thickness 4 μm. Parafinized histological samples were stained with H/E and studied immunohistochemically, with mAb against OCT4. Then measured area of different types of SB using the program cellSens Standard.

**Results:** OCT4positivityappearedgenerallyamongSEMS.Bysizesand histological characteristics, SEMS classified into three types: reparative, neoplastic and Cancer. The average area of reparative SEMS was 1141.1 ± 305.0 mkm2, the average area of neoplastic SEMS was 2553.9 ± 656.2 mkm2, the average area of cancer SEMS was 2553.9 ± 656.2 mkm2. Reparative SEMS distributed frequently among chronic cervicitis and L-SIL samples, while neoplastic SEMS showed significant positivity among the samples of L-SIL and H-SIL, cancer SEM Samong carcinoma samples with distinguishable atypical polymor- phic nucleus.

**Conclusion:** Different types of SEMS have their morphometric characteristicsas well as immunohistochemical and, which may be used for differential diagnosis of HPV associated uterine cervical pathologies.