Management of inflammatory bowel disease in pregnancy – clinical series

Managementul bolii inflamatorii intestinale în sarcină – serie de cazuri clinice

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Inflammatory bowel diseases (ulcerative colitis, Chron disease and indeterminate colitis) affect mainly women of childbearing age, resulting in a challenge in obtaining a pregnancy. A quiescent or a good controlled disease before pregnancy and adequate family planning represent a desideratum. Subsequent monitoring of pregnant women with inflammatory bowel disease (IBD) should be multidisciplinary, involving gastroenterologists, obstetricians and neonatologists, with a good knowledge of all pathophysiological implications and the adequacy of the therapeutic plan. The advances in IBD treatment during pregnancy and lactation have resulted in a better materno-fetal outcome. Weak control of the disease correlates with specific complications, such as miscarriage, premature birth, insufficient intrauterine growth, preeclampsia, C-section, and low Appar score at birth. The association between inflammatory intestinal disease, its treatment and the occurrence of fetal malformations remains controversial, although numerous studies have been conducted to verify this aspect. The use of biological therapy in inflammatory bowel disease in pregnancy has led to a better disease control, but has brought new challenges for obstetricians and neonatologists, in particular due to the possible immunosuppressant syndrome of the newborn. This issue is being discussed with interest by international organizations, and at the European level there is a therapeutic consensus on fertility, pregnancy and breastfeeding in patients with intestinal inflammatory disease. We present a series of cases of inflammatory bowel disease in pregnancies which were addressed to our clinic and the correlation between the disease and the maternofetal outcome.

Keywords: pregnancy, treatment, inflammatory bowel disease, fetal outcome

Testing for TORCH infections in pregnant women from Hospital of Obstetrics and Gynaecology of Ploiești, Romania

Testarea pentru infecțiile TORCH la femeile gravide din Spitalul de Obstetrică și Ginecologie din Ploiești, România

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Objective. In this paper, we want to highlight, on the one hand, the importance of preventing the vertical transmission of TORCH-associated materno-fetal infections by promoting the voluntary counseling and testing of women of childbearing age in order to raise the awareness of the risks involved in these infections and, on the other hand, the early diagnosis of the infections, so that pregnant women can benefit from obstetrical monitoring and adequate intranatal and postnatal care. **Materials and method.** The study was conducted by applying a questionnaire to a group of 400 pregnant women who gave birth at the Obstetrics and Gynecology Hospital from Ploiești during June-September 2018. **Results.** 190 of the respondents (47.5%) were tested for toxoplasmosis, 120 out of 400 (30%) were not tested, and 90 (22.5%) did not know if they were tested for toxoplasmosis. 160 out of 40 respondents were tested for cytomegalovirus (CMV) infection, 120 out of 40 respondents were not tested, and 120 out of 40 respondents did not know whether they were tested. Of the 400 respondents, 42% were tested for herpes simplex viral infection, 28% were not tested, and 30% did not know if they were tested. 210 out of 400 participants underwent detection of IgG anti-Rubella antibodies, 210 of the 400 respondents were tested for IgM anti-Rubella antibodies, 20 of the 400 responses performed other tests, and 170 out of 400 respondents did not know what tests they did. **Conclusions.** The lack of resources and inadequate maternal care are in the way of effective programs. Many of these interventions could be more effective, not only by better understanding of the epidemiology and impact of illness by future mothers, but also by improving prevention, particularly through the education of the population. Congenital rubella can be prevented by immunizing women of susceptible, fertile age, before they become pregnant. The identification of newborns with congenital CMV infection or toxoplasmosis allows the treatment to reduce the harmful effects.

Keywords: TORCH, pregnant, risk factors, congenital infections



The necessity and the call upon of urgent introduction in the Romanian obstetric practice of the Robson criteria

Necesitatea și obligativitatea introducerii urgente în practica obstetricală românească a criteriilor Robson pentru indicația operației cezariene

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In modern obstetrics, where the C-section index in Bucharest reaches and sometimes even exceeds 85% in some maternities, and ranges from 45% to 50% in the other university medical centers of the country, we fairly ask ourselves at least a few questions:

- How many of these caesarean sections have actual indications?
- How many of them are, in fact, caesarean sections at the patient's request or caesarean used for defensive purposes by obstetricians?
- How do we explain the extremely high territorial variability of this index in Romania?
- What are the causes, the short-, medium- and long-term implications of these practices?

■ Which of the indications used are real and how frequently are some indications used? Why?

The civilized world of obstetrics, the one we aspire to in Romania, has long put these natural questions, and one of the solutions that can lead to pertinent answers on this issue is the urgent **introduction into the obstetrical practice of the ten criteria and of the Robson caesarean section classification system.** In fact, this use has long been a WHO recommendation.

Keywords: caesarean section, Robson criteria for caesarean section, indication of caesarean section, caesarean section at request, defensive caesarean section

Pregnancy outcomes in complex genital tract malformations

Rezultatele sarcinii în malformațiile complexe ale tractului genital

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Introduction. The group of vertebral-anorectal-renal anomalies identified in certain patients exhibits one potential VACTERL spectrum. The association with class IV müllerian anomalies widens the clinical phenotypic heterogeneity. However, the medical literature provides only one case report on the coexistence of VACTERL association with distal vaginal atresia and a partial bicornuate uterus in a virgin woman. There is scarce information regarding the rate of fertility and the obstetrical outcomes of patients diagnosed with complex urogenital and anal malformations. Case description. We present a meta-analysis of pregnancy outcome in genital tract malformations. Also, we present a particulare case of an 18-years-old woman, gravida 0, para 0, with a history of 5-month amenorrhea who was admitted via the emergency department of our institution on 24.09.2017 in a post-exploratory laparotomy status with altered general condition, with the main complaint of abdominal pain. The patient's medical and gynecologic history revealed the presence of a complex vertebral, lower gastrointestinal tract and urogenital malformation association comprising of scoliosis, anal atresia, as well as malposition of the right kidney, rudimental labia, distal vaginal atresia and complete bicornuate uterus, for which the patient underwent multiple surgical procedures of vaginoplasty and anoplasty. The patient was stable at the moment of the admission in our clinic. The CT exam confirmed the association of vertebral-anorectal-renal and müllerian anomalies, and showed a retroperitoneal 21-week dead fetus. The emergency laparotomy performed in our department revealed enlarged right and left hemiuterus with no gestational sac present in any uterine cavity after histerotomy. Total histerectomy of the left hemiuterus is performed due to persistent bleeding along with left adnexectomy. The presence of the retroperitoneal macerated fetus along with the placenta was identified at the opening of the vagina; both were removed and sent to hystopathological examination. The postoperative evolution of the patient was favourable and 7 days later the discharge documentation was made. **Conclusions.** The identification of müllerian anomalies should grant clinicians with a high index of suspicion for other associated urinary or gastrointestinal malformations. Despite favorable results in reconstructive surgery, urogenital anomalies remain meaningful obstetrical challenges, their therapeutic management becoming increasingly controversial. In these circumstances, a multidisciplinary surgical approach provided in a tertiary medical unit becomes compulsory. The pregnancy outcome is severly impaired in cases of complex genital malformations with other associated anomalies, but the contribution of the latter to these unfavourable results is yet to be fully explored.

Keywords: genital tract malformation, VACTERL anomalies, pregnancy outcome

Brugada syndrome – conduct in pregnancy

Sindromul Brugada – conduita în sarcină

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In the context of ongoing progress in all medical fields, more and more special situations occur in the care of pregnant women. There are more and more complex problems and challenges regarding the evolution of pregnancy, maternal resonance, and fetal prognosis. Such an example is Brugada syndrome. In this case, the obstetrician follows

a series of very delicate decisions, such as monitoring the cardiac pathology and pregnancy surveillance, setting the time and way of birth, working with cardiologists and anesthetists, and so on.

Keywords: Brugada syndrome, high-risk pregnancy, sudden death, pregnancy-associated pathology

Considerations about multidisciplinary therapeutic approach for STUMP uterine tumors Abordarea terapeutică pluridisciplinară a tumorilor uterine de tip STUMP

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Introduction. The abbreviation of "STUMPs" indicates the smooth uterine muscle of uncertain malignant potential tumors, from the group of uterine smooth muscle tumors (SMTs) that cannot be diagnosed unequivocally as benign or malignant. The diagnosis, the medical approach and the follow-up of this pathology are still controversial. Materials and method. We reviewed the medical databases using the MeSH words "STUMPs", "smooth uterine muscle tumors", or "SMTs" to highlight the most important publications on this topic. **Results.** The literature research revealed 162 articles about "STUMPs". The majority are case reports or case series, including less than 10 patients with long-term follow-up. The preoperative imaging STUMP diagnosis or differentiation from leiomyoma-leiomyosarcoma is difficult. The preoperative sonographic tumors appear in 83.3% with welldefined margins, 66.7% hyperechoic, 100% heterogeneous and 66.7% acoustic shadowing. The patient's age, fertility desire, imagistic characteristics, size and location of tumor should be considered before the procedure. The pathologic features expressed mean number of mitosis about 8, mild atypia almost 66.7% and necrosis in 33.3% cases. The recurrence rate after myomectomy was reported as 6.6%. After STUMP diagnosis, there can be performed second myomectomy or hysterectomy. Other treatment options for recurrence include adjuvant chemotherapy, radiotherapy and progestins GnRH analogs. **Conclusions.** STUMP is classified as an intermediate form, histopathologically between benign or malignant uterine tumors. Metastasis after many years from initial approach can be seen, and patients diagnosed with STUMP should be followed on long term.

Keywords: myometrial tumors, smooth uterine muscle tumors, uncertain malignancy

Maternal allergen-specific IgG may protect the child against allergic sensitization – literature review IgG specifice alergenului matern pot proteja copilul împotriva sensibilizării alergice –review de literatură

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Background. The analysis of allergen-specific IgE responses in birth cohorts with micro-arrayed allergens has provided detailed information regarding the evolution of specific IgE responses in children. Data regarding the early development of allergen-specific IgG are needed. **Method.** We analyzed the results obtained by searching for keywords "maternal allergens", "specific IgG", and "sensibilisation" in PubMed database and Elsevier. There were identified a number of 1984 publications, of which we detained exclusively those *in extenso* describing results of randomized studies. The studies were analyzed in order to identify the following variables: specific IgG dosage of maternal allergen in the third trimester, the identification of IgG in cord blood, and allergic reactions of children at 2 months, 6 months, 1 year and 5

years. **Results and discussion.** A number of two studies have identified the fact that all children from mothers with elevated (>30 ISU) specific plasma IgG against an allergen did not have IgE sensitivity against that allergen at the age of 5 years old. **Conclusions.** The latest studies in the field have shown that high levels of IgG specific to allergen in mothers during the third trimester and in cord blood seem to protect against allergic sensibilisation in children. This finding has clinical implications for the prevention of allergies, as well as in their treatment. Studies on human subjects are limited, but the experimental ones are promising, and more studies are needed on this topic.

Keywords: IgE response in children, IgG, maternal allergens



Lateral uterine suspension in the treatment of pelvic organ prolapse – the experience of Bucharest University Emergency Hospital

Suspensia laterală laparoscopică în tratamentul prolapsului vaginal – experiența Spitalului Universitar de Urgență București

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Pelvic organ prolapse has become a common pathology among women, and due to the increased incidence of this disorder, multiple surgical techniques have been developed as a means of treatment. There are multiple causes for pelvic prolapse. One of the main causes is increased intraabdominal pressure that can be caused by pregnancy, labor, birth or obesity. Other causes include hysterectomy, pelvic trauma and connective tissue disorders. Many hypotheses claim that the uterus itself is a healthy organ, and the pathophysiology of prolapse is a congenital or acquired connective tissue disorder (during vaginal delivery) and that uterine prolapse is just a symptom, not a disease. Vaginal hysterectomy fails to address the pathology in connective tissue disease, which causes recurrence in 10-40% of cases.

Laparoscopic lateral suspension is a surgical technique which has the following key surgical steps: vesicovaginal dissection, mesh insertion and fixation, and the lateral suspension itself. The main advantages of this technique are uterine preservation and low recurrence rate. Other advantages include the low risk of intraoperative nerve and vascular system injury, the reduction of hospitalisation, as well as the simplicity of the technique. The complications of the technique are mesh-related, that can cause erosion, infection, pain and perforation of neighboring organs. The laparoscopic lateral suspension is an alternative treatment in vaginal prolapse, with few complications and with the advantage of uterine preservation.

Keywords: vaginal prolapse, laparoscopic lateral suspension

Ichthyosis uteri associated with *in situ* squamous carcinoma. Case presentation Asociere ichthyosis uteri – carcinom scuamos in situ. Prezentare de caz

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A 62-year-old Caucasian woman, in menopause for 15 years, is assessed for vaginal bleeding, and diagnosed by vaginal sonography with atrophic endometrium. Because of atypical endometrial cells in vaginal cytology, it is decided and done a total hysterectomy, with bilateral adnexectomy. The postoperative microscopy depicted extensive ichthyosis of the entire endometrium, with extensive superimposed high-grade dysplastic changes associated. Additionally, the squamous epithelium of the cervix showed minimal pathological changes. *Ichthyosis uteri* is a very rare condition, defined as squamous metaplasia of the surface endometrium. There are discussed the potential genesis

of these findings, and also the neoplastic potential of *ichthyosis uteri*. The replacement of the endometrium surface by stratified squamous epithelium is secondary to a variety of inflammatory endometrial conditions, such as chronic pyometria, endometritis, intrauterine contraceptive devices or caustic substances. It is concluded that there was a dysplastic evolution of a preexisting *ichthyosis uteri*, limited to endometrial cavity. The possibility of malignant evolution of *ichthyosis uteri* should be considered when plaques of squamous epithelium with dysplastic changes are identified in an endometrial biopsy or curettage.

Keywords: ichtyosis uteri, in situ squamous carcinoma

Association between preterm birth and genital colonization with *Mycoplasma* Infecția cu Mycoplasma în determinismul nașterii premature

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Preterm labor is liable for most cases of neonatal death. In most of these cases, the causes have not been established, although several risk factors have been incriminated. *Mycoplasma hominis* is a common vaginal organism associated with bacterial vaginosis. The bacterium is considered inoffensive for the most part in nonpregnant women, but it can cause intraamniotic infections, which are associated with inflammation, preterm premature rupture of membranes, and preterm birth. The role of these genital tract habitants in the infection during pregnancy and their capacity to

invade the placental and fetal tissue are discussed. Especially, the role of some of these organisms in prematurity may be mechanistically associated to their ability to induce inflammatory cytokines, thus triggering pathways causing to premature labor. A review of this intensifying research of mycoplasmas in relation to pregnancy led to several questions and findings that will be important to examine in future research.

Keywords: preterm birth, genital mycoplasmas, microbial invasion of the amniotic cavity

Optimizing ovarian response in patients with poor ovarian reserve – update

Optimizarea răspunsului ovarian la pacientele cu rezervă ovariană scăzută – update

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Counseling patients with low ovarian reserve is difficult, because of the contradictory views that exist so far in the literature. This is largely due to the lack of uniform criteria for establishing low ovarian reserve diagnosis. In 2011, the Bologna criteria were developed to diagnose this pathology, but many clinicians do not accept them as valid, or consider them to be insufficient. Although nearly 40 years have passed since the birth of the first child by *in vitro* fertilization procedure, women with low ovarian reserve remain a group of patients

difficult to handle with. Despite the efforts made to improve pregnancy rates, they have not changed significantly. Lately, studies have focused on topics such as luteal phase stimulation, mitochondrial study, platelet-enhancing platelet-supplementation, growth hormone supplementation, androgens, Q10 coenzyme or myo-inositol. We review the latest news in this area, hoping to find the right tools to fight low ovarian reserve.

Keywords: poor ovarian reserve, poor responders, ovarian stimulation, luteal phase ovarian stimulation

Laparoscopic treatment of pelvic inflammatory disease and infertility implications Implicațiile tratamentului laparoscopic în tratarea bolii inflamatorii pelviene

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Introduction. Genital infections, in both men and women, may cause permanent functional damage to the reproductive tract, resulting in infertility. In men, post-infection infertility is uncommon, whereas in women sequelae after pelvic inflammatory disease (PID) are the most common cause of acquired infertility. Objective. To assess if laparoscopy can improve the outcome in term of infertility in patients with pelvic inflammatory disease. Materials and method. We conducted a descriptive retrospective cohort study in our clinic (Bucur Maternity from Bucharest) between 2016 and 2018 among patients who were admitted for PID. Patients age, parity, the anatomoclinical form of the disease, the presence of infertility before and after treatment, the type of surgery and the outcome were assesed. Results. 267 patients with PID were admitted in the three years studied. Fourty-three underwent

surgery, of which 18 were laparoscopic. Five patients (28%) suffered from primary or secondary infertility prior to surgery. Almost half of the laparoscopies were performed for unilateral or bilateral sactosalpinx; there were two cases of both endometriosis and PID, two cases of adnexal tumors, one case of bilateral pyosalpinx, and one case of haematosalpinx. The evolution was uneventfull in all cases. The patients were followed for a mean period of 12 months after surgery, and hysterosalpingography was performed in order to asses tubal patency. We encountered tubal obstruction in 60% of the cases where tuba were preserved. **Conclusions.** Minimally invasive surgery is justified in order to dignose, treat and prevent further fertility implications in patients with PID.

Keywords: pelvic inflammatory disease, infertility, laparoscopy



Prolactin and pregnancy – from pituitary physiology to prolactinoma

Prolactina și sarcina – de la fiziologia hipofizei la prolactinom

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Introduction. Prolactin (PRL) is a key hormone for pregnancy and lactation. The wish to conceive is related to its normal levels, since it blocks the FSH-LH-ovarian pathways. Prolactinoma is a benign tumour correlated with infertility+/-galactorrhea. PRL is the most frequent abnormal secretion among hypophyseal panel. Aim. We introduce general data regarding PRL intra- and postpartum. **Data.** During pregnancy, the pituitary gland increases its volume up to 2-3 times to prepare the breast for lactation via PRL which progressively increases, thus the first diagnosis of prolactinoma during pregnancy is difficult (moreover, an untreated prolactinoma has an extremely low rate of spontaneous fertility). The cases priorly diagnosed with a PRL-producing tumour are responsive to dopamine agonists (DA) as bromocriptine and cabergoline. DA should not be stopped until the confirmation of pregnancy, since there is not an associated higher risk of miscarriage, premature birth, multiple births, and congenital malformations (in-

cluding studies that followed the newborn until pubertal time). The rate of tumour increase during pregnancy depends on diameter: for microadenomas it is 2-3%, for macroprolactionomas it is 20-30%. In this particular case, if suspected a dangerous tumour expansion, visual field should immediately be checked. Also, magnetic resonance imagery without contrast may be used if useful. Once the expansion is confirmed, DA is reinitiated or, in selected case, neurosurgery is needed. After birth, the breastfeeding in prolactinoma is allowed, delaying DA. Also, in cases with macroprolactinomas, if an extension is suspected, a pituitary imagery and a visual control represent the first approach. **Conclusions.** Considering the dynamic changes of PRL during pregnancy and lactation, the patient diagnosed with prolactinoma needs a special follow-up, but generally a good prognosis is expected, unless exceptionally large invasive tumours suffer an expansion.

Keywords: prolactin, pituitary, pregnancy

Caesarean complicated with distance endometriosis

Cezariană complicată cu endometrioză la distanță

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Introduction. Abdominal wall endometriosis (AWE) represents a rare event, yet its frequency is increasing lately due to a higher number of caesarean sections. This is considered a late complication after pregnancy period. Aim. We introduce an overview regarding AWE. Method. This is a general introduction of literature data. The level of statistical evidence remains the series of cases. An example of a case report is also introduced. **General data.** The diagnosis of AWE is established within weeks up to years after birth. The clinical clues are mostly related to local pain; even the relationship with cyclic monthly menses cannot be clearly established. The atypical localization of the pain as lumbar or leg cramps has been described. Also, the palpation of a tumour at the level of abdominal wall is possible in less than one third of patients. The ultrasound of abdominal wall, as well as computed tomography and/ or magnetic resonance imagery represent the best imagery tools. Fluorodeoxyglucose positron emission tomography – computed tomography might be used, but since the turnover rate of the underlying cells is low, the method may bring falsely negative results. Surgery is necessary in each case. In most situations, the procedure is successful and uneventful. The risk of malignant transformation has been described in a few cases, but it is low. The recurrence also has been reported if the endometrial cells are not completely removed. **Discussion.** There is still a matter of debate which is the pathogenic loop of the implant, and also the risk factors of AWE or its reoccurrence are unknown until this moment. Neither are the contributors to sarcomatous transformation. **Conclusions.** AWE is a challenging pathogenic condition with an increasing incidence in the last decades.

Keywords: endometriosis, abdominal wall, caesarean

Myometrium changes after arterial embolization for uterine fibroids

Modificările miometrului după tratamentul fibromului uterin prin embolizare

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Introduction. Embolization of uterine arteries (UAE) or embolization of uterine fibroids (EFM), a technique used in the treatment of uterine fibroids for the last several decades, has also become more and more used in our country. Although there is still a relatively small number of medical units, public or private, where it is practiced, the number of cases treated by this method has increased significantly in recent years, so this has allowed the accumulation of data based on our own experience. **Presentation of four cases.** We selected for presentation four cases that underwent uterine surgery in the Bucur Maternity after prior embolization of the uterine arteries. In three of these four cases it was performed hysterectomy, and in

one case it was performed myomectomy. The characteristic feature of the histopathological examination was diffuse fibrosis in the thickness of the uterine wall, thickened vascular structures and intraluminal amorphous material with perivascular infiltration with multinucleated giant histiocytes around the foreign body – the histological aspect of nonspecific granulomatous inflammation with giant cells. **Conclusions.** The embolization of the uterine arteries may cause a giant-cell type inflammation at the level of the myometrium, and this type of change could be the cause of a poor prognosis for women who want a future pregnancy.

Keywords: mioma, embolization, inflammation

Ovarian rejuvenation with PRP (plasma rich in platelets) – a therapeutic alternative in the treatment of women's infertility

Rejuvenarea ovariană cu PRP (plasma rich in platelets) – o alternativă terapeutică în tratamentul infertilității feminine

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Many women try to become pregnant at older ages and there are even a lot of couples with unexplained infertility; for all these case we have to consider the status of their quality of embryos. This means that the lower the quality of eggs they have, the bigger the dilemma whether to use their own eggs in in vitro fertilization (IVF) technologies that they usually go in order to obtain successful pregnancies. New scientific attempts have been made nowadays in order to regenerate their ovarian tissue, and so they can have more possibilities for a successful pregnancy. PRP (plasma rich in platelets) is a natural product where a high level of platelets is concentrated, but with growth factors concentration three to five times greater than plasma. PRP contains cytokines which play an important role in cellular proliferation, chemotaxis and differentiation of mesenchymal and other cells and promote angiogenesis. We try to use the injection of the PRP to the one/two ovaries by laparoscopy in seven cases of women with unexplained infertility or poor responders to ovarian stimulation protocols. Then AMH (anti-müllerian hormone), FSH, LH and estradiol levels are measured at monthly intervals in women who do not menstruate, and during the menstrual flow in menstruating women for a period of six months. If the AMH levels rise, while the FSH, LH and estradiol levels become lower, there is an objective evidence of ovarian rejuvenation. We had one spontaneous pregnancy two months after the procedure and improved hormonal status in four cases of poor responders. These encouraging results should extend our pilot study and should also focus the injections by testing inhibin's B levels after PRP's infusion monthly, because this protein is the one that gives information about eggs' quality. It seems like the ideal candidates for ovarian regeneration with PRP are the following: menopausal or perimenopausal women under the age of 50, infertile women who are over the age of 35, having low egg reserve and low AMH, women under the age of 35 who have low egg reserve and low AMH levels, women with premature ovarian failure (POF), and women with idiopathic infertility over 35 years old.

Keywords: ovarian rejuvenation, plasma rich in platelets, infertility



Placental chorioangioma. How does it affect the perinatal outcome?

Corioangiomul placentar – cum afectează prognosticul obstetrical?

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Placental chorioangioma is the most common benign non-trophoblastic tumor of the placenta, arising from primitive chorionic mesenchyme. It is a relatively rare condition (occuring in approximately 1% of pregnancies) that results in serious prenatal complications and adverse pregnancy outcome. While small chorioangiomas tend to remain asymptomatic, the large ones (arbitrarly defined as measuring over 4-5 cm in diameter) have been associated with fetal anemia, hyperdynamic heart strain, hydrops,

growth restriction, polyhydramnios, and maternal mirror syndrome. We present the case of a large placental chorioangioma (10 cm) which was diagnosed prenatally by ultrasound examination and had no impact on fetal development, resulting in a successful delivery at term, which is a rare situation. We also review the literature regarding the management and perinatal outcome in pregnancies complicated by these rare tumors.

Keywords: chorioangioma, perinatal outcome

The fractional microablative CO₂ laser for the treatment of menopausal vulvovaginal atrophy – how effective is it?

Laserul CO₂ fracțional microablativ în tratamentul atrofiei vaginale din menopauză – cât este de eficient?

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Objectives. This article reviews the literature regarding the efficacy of the use of pulsed CO₂ laser for the treatment of vulvovaginal atrophy (VVA) in postmenopausal women. **Method.** Eleven studies, involving more than 1500 participants, were included in this systematic review. All patients received three laser sessions, one at every 4-6 weeks. All studies included examinations at baseline, then one after each session. Some studies included evaluation at follow-ups at 3, 6, 12, 18 and 24 months. We selected the studies based on the same evaluation scales: Visual Analog Scales (VAS), Vaginal Health Index Scores (VHIS), Female Sexual Function Index (FSFI) and Short Form 12 questionnaires (SF-12). The participants' satisfaction was measured on a five-point Likert scale (1=very dissatisfied; 5=very satisfied). These scales were used to assess pain, vaginal burning, vaginal itching, vaginal dryness, dyspareunia, and dysuria. We added three studies based on histological

and microscopic effects as well. **Results.** Data indicated in all available publications a significant improvement in VVA symptoms (vaginal dryness, burning, itching and dyspareunia) (p<0.001) and overall, after three sessions, 92.58% of patients were satisfied or very satisfied. In the long-term studies, the satisfaction of the patients at six months was 92%, at 12 months it was 82.66%, at 18 months it was 63% and at 24 months it was 25%. The objective histological measurements of the effect of laser therapy improved significantly as well. **Conclusions.** Histological and clinical increasing evidence support the use of CO_2 lasers in the treatment of VVA. Long-term data showed that the improvement of vaginal health continues up to 12 months after fractional CO_2 laser treatment, and progressive decreses up to 24 months.

Keywords: vulvovaginal atrophy, CO₂ laser, menopause, dryness

Microbiological aspects of the endometrium in primary infertility

Aspectele microbiologice ale endometrului în infertilitatea primară

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Introduction. The human microbiome has gained much attention recently for its role in health and diseases. The endometrial factor and specifically the microbiological view have long been neglected in reproduction, because it was considered an old concept with no potential improvment. In the last decade, important discoveries, led by improving technology, have been made in the study of microbial communities not only in the vagina, but also in the endometrial cavity and its implication in reproductive health and disease. **Aim of the study.** To assess the endometrial microbiome in primary infertility patients. Materials and method. We provided a prospective study, which included 96 patients divided into two groups. The study group included 48 patients with primary infertility and the control group (48 fertile patients). In both groups we performed endometrial biopsy in the proliferative phase with Pipelle endometrial suction curette. The study was approved by the Research Ethics Committee of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, Chişinău, Republic of Moldova (No. 79/62 of 26.04.2017). The patients have signed the informed

consent to participate in the research. All data management and analyses were performed using SPSS 20 and Microsoft Excel 2016. **Results.** The mean age of the patients in the study group was 29±4.58 years old, and in the control group 29.2 ± 4.29 years old (p=0.801). În the study group, the duration of infertility was mostly: two years (20.8%), three years (22.9%), and more than five years (27.1%). The most representative bacterium in the endometrium of the patients with primary infertility was *Lactobacillus* spp. (75%), χ^2 =0.236; p=0.627; followed by *Ureaplasma urealiticum* + parvum in 37.5%, χ^2 =13.714; p<0.001; Atopobium vaginae – 25%, χ^2 =1.640, p=0.20; *Enterobacteriaceae* – 18.8%, χ^2 =9.931, p=0.002. **Conclusions.** In our study, we demonstrated that the endometrium is populated by a number of bacteria, and that their composition and quantity differ in fertile patients and in those who suffer from infertility. This demonstrates that the endometrial microbiome has an important impact in reproduction.

Keywords: endometrium, primary infertility, endometrial microbiome, microbiome in reproduction

Modern management in cervical cancer Actualități în cancerul de col uterin

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Introduction. Cervical cancer is an important public health issue, with an increased mortality rate. It ranks second in Europe in female population, after breast cancer, and is more common in young women, representing the second most frequent malignancy in pregnancy (after breast cancer), with an estimated incidence of 0.8-1.5 cases in 10,000 births. The detection of cervical neoplasm is facilitated by the introduction of cytology as screening. Thus, 1-3% of women diagnosed with cervical cancer are pregnant or in first six weeks postpartum at the time of diagnosis. Materials and **method.** The diagnosis of cervical cancer in pregnant women requires a therapeutic attitude guided by the patient's desire to maintain or interrupt pregnancy, gestational age and the clinical stage of the disease. In advanced stages, the treatment is similar to that of nonpregnant patients. If pregnancy is ≥ 20 weeks of gestation, it is recommended to evacuate the uterus (medically or surgically) before chemo- and radiotherapy. In pregnant women with early staged cervical cancer, radical hysterectomy is recommended with the fetus *in situ* and ovarian sparring if possible. In pregnant women who opted for continued pregnancy, the curative treatment begins at birth or postpartum. The approach is different, depending on the desire to preserve fertility. **Conclusions.** Preserving ovarian function in patients with cervical neoplasm is a matter of medical and emotional interest, as well as the quality of life for young women who want to procreate. Successful births after *in vitro* fertilization, and ovarian stimulation with oocyte sampling for transfer to surrogate mothers have been described in cervical cancer patients, but this process delays the onset of radical radiotherapy.

Keywords: cervical cancer, fertility preservation, neoadjuvant therapy



Risk markers for cervical cancer

Markeri de risc pentru cancerul cevical

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Background. The understanding of the molecular changes during HPV persistence leading to CIN3 and early cancer has provided more accurate biomarkers for diagnosis, prognosis and treatment options. There is evidence that fuller HPV genotyping and variant HPV classification provide additional information to support the risk stratification. The sensitivity of dual-staining p16/Ki67 versus Pap cytology was significantly higher, whereas specificity was equivalent. The molecular test quantifying E6/E7 oncogene expression and detection of the oncoproteins E6/E7 can be used to identify progressive lesions. Methylation of host and viral regions of HPV has high sensitivity for CIN3, and could predict which CIN2 progress to CIN3 and detect all cervical cancers years before the diagnosis. The next generation sequencing can identify several potential biomarkers such as variant HPV classification, HPV sta-

tus (integrated, episomal or absence), somatic mutations and the associated genome rearrangements. **Results.** The risk of precancer and cancer varies substantially for different carcinogen HPV types, HPV 16 being associated with the highest risk. The types 18, 31, 33, and 45 carry a much higher risk than other types; the types 39, 56, 59, and 66 carry lower risk and could be designated as intermediate risk. 100% of cases of CIN2+ lesions are positive by using dual-staining p16/Ki67 test, but the specificity was lower. Also, all cases of CIN2+ lesions are positive by using mRNA detection, but we have a small number of cases. **Conclusions.** These biomarkers of premalignant phase of carcinogenesis could help to avoid the overtreatment of lesions that spontaneously regress and to better target the lesions requiring treatment.

Keywords: molecular markers, cervical lesions

Principles of enhanced recovery after surgery (ERAS)

Principiile refacerii facilitate după intervenția chirurgicală (ERAS)

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Enhanced recovery after surgery (ERAS) protocol represents a new concept in the field of surgical specialties, including caesarean section. It is based on the implementation on already known principles, others reevaluated, integrated into a new concept which has as end point the shorting of hospital stay, lower surgical complications and lower costs of health care. It is beneficial for both patient and health system. Protocols have been developed and implemented for colorectal surgery, gynecologic oncology, caesarean section and

spreading continues to other surgical specialties. The basic elements of ERAS concept are: preoperative education, avoiding mechanical bowel preparation, perioperative euvolemia, antibiotics and thromboembolic prophylaxis, standard anesthetic protocols, avoiding gastric suction postoperatively, early removal of urinary drainage, early ambulation and short hospital stay (2.5 days).

Keywords: preoperative diet, mechanical bowel preparation, skin preparation, euvolemia, normothermia, analgesia

Complementary therapies in infertilty – benefits and limits

Terapii complementare în infertilitate – beneficii și limite

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Introduction. In complementary medicine (phyto-, gemmo-, aroma-, apitherapy, and traditional Chinese medicine, Ayurvedic medicine) we can find valuable items that can be used in conjunction with those promoted by allopathic medicine. These therapies have the advantage of an integrative approach. Feminine infertility is the result of a combination of dysfunctions that must be approached logically at each system level (dysfunction of the hypothalamic-pituitary-ovarian axis, whether or not associated with an infectious-inflammatory factor, endometriosis, adrenal, hepatic and/or digestive dysfunction). In Romania, the control of non-registered plant products at the National Medicines Agency is only done at the Ministry of Agriculture (they are considered food supplements) and is done less rigorously, without complying with the European Pharmacopeea standards. These products are being used more and more by our patients. Materials and method. We present some useful data to the practitioner gynecologist in the therapeutic approach of the infertile couple, based on the data from literature and personal practice. **Results.** Plants used in infertility therapy can be grouped in plants with hormonal

effects (estrogen-like, progesterone-like or central nervous and hormonal regulator effect), plants with antiinflammatory effect, antiinfectious effect, and venous drainage. A special category are the so-called plants with adaptive effects, both stimulating and inhibiting hormonal secretions, as well as plants with complex effects on the female genital apparatus. Another class are the gemmotherapeutics, hydro-glycero-alcoholic extracts from the embryonic tissues of plants (buds, plants, branches etc.). The indications, as well as the contraindications of these types of treatment must be known. The marketing of complex preparations with insufficiently verified doses or sometimes illogical combinations may become dangerous for patients. **Conclusions.** We advocate the use of complementary treatments associated with classical treatments. The practitioner gynecologist can work with a specialist in complementary therapies to significantly improve prognosis in rigorously diagnosed cases, but in turn it is good to be informed about the real benefits, but also about the limits of these therapies.

Keywords: infertility, complementary medicine

Stage IIb cervical cancer – primary surgical treatment versus radiochemotherapy

Cancerul de col uterin în stadiul IIb – tratament chirurgical primar versus radiochimioterapie

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Cervical cancer is one of the most frequent neoplasias, ranked second in malignant tumors among women worldwide. In Romania, the main form of cancer among women is cervical cancer (67% of genital cancers) and is the second cause of death by cancer. Screening programs include clinical examination and cervical cytology, with the aim of early diagnosis, and reduction of morbidity and mortality through cervical cancer. Currently, the main standard of treatment for cervical cancer stage IIb is radiotherapy associated with chemotherapy. There are numerous studies demonstrating that the clinical staging IIb is sometimes overestimated due to inflammation at the level of the parameters, causing an incorrect assessment as tumor invasion in the parameters.

Taking into consideration this overstaging, the radical hysterectomy with pelvic and paraaortic lymph node dissection may be the first treatment. The most important prognostic factor is the involvement of pelvic nodes. The survival rate is not significantly influenced if it involved only the parametria. The role of surgical treatment *per primam* is the proper staging of cervical cancer, so that the radiochemotherapy treatment is at lower doses. Also, another advantage of the radical hysterectomy with pelvic and paraaortic lymph node dissection is the decrease of radioresistant tumor in cervical cancer by excision of the primary tumor, and also the decrease of morbidity due to radiotherapy.

Keywords: cancer, cervical, treatment, radical, hysterectomy

Pregnancy before surgery or surgery before pregnancy in patients with deep infiltrative endometriosis?

Sarcina înaintea chirurgiei sau chirurgia înaintea sarcinii la pacientele cu endometrioză profundă infiltrativă?

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Deep infiltrative endometriosis (DIE) is a particular form of endometriosis characterized by lesions with a depth greater than 5 mm, with typical locations such as rectovaginal fascia, uterosacral ligaments, Douglas cul-de-sac, but also with the involvement of important organs, such as bowels, ureters and bladder. Constant dillemas regarding the management of women with DIE who want to become pregnant appear due to the lack of randomized control trials from the guidelines for endometriosis. The confusing decisions whether to perform a surgery before or after the assisted-reproductive technique (ART) comes from the major two symptoms of the patients with endometriosis: pain and/or infertility. The guidelines give a suggestion that not all the women with DIE require ART, and surgery is more often performed when a patient has painful symptoms. The failure of ART could also appear before and after the surgery, due to the impairment of immune system response or hormonal disfunctions encountered in endometriosis. The situation is more complicated when the patient's condition associates endometrioma and the radical surgery will only reduce the ovarian reserve, worsening the pregnancies rates. Moreover, when the endometriosis lesions interest the colorectal area, the best therapeutic decision would be to involve a multidisciplinary team, especially a general surgeon. Several studies showed that ART preganancies in women with infertility improved after performing laparoscopic excision of DIE, while other studies stated the opposite. Today, no definitive strong recommendation can be provided regarding the management of these patients, randomized controlled trials being the only studies that could give a definitive answer.

Keywords: deep-infiltrative endometriosis, pregnancy, assisted-reproductive techniques



The quality of life in patients with deep infiltrative endometriosis who underwent colorectal laparoscopic resection

Calitatea vieții la pacientele cu endometrioză profundă și rezecție colorectală laparoscopică

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Objective. The aim of this paper is to present the authors' experience and to evaluate the effectiveness of laparoscopic colorectal resection in cases with deep infiltrating endometriosis, as well as the impact on the quality of life, symptomatology and digestive symptoms. Materials and method. During June 2017 until January 2019, a number of 120 patients underwent laparoscopy for deep infiltrative endometriosis. Fourty-two patients with deep endometriosis were included in the study – all the patients included in the study completed a questionnaire on the symptoms of preoperative endometriosis and quality of life (Questionnaire SF-36), and completed the preoperative evaluation (MRI, transvaginal ultrasound, endo-rectal ultrasound, HidroColo-CT). The status and quality of life were assessed postoperatively. The gynecological and digestive symptoms, as well as the rate of perioperative complications were also evaluated. The laparoscopic surgery was performed by the same surgical team in all cases. **Results.** Twenty patients (47.62%) benefited from laparoscopic segmental rectosigmoid resection with end-to-end mechanical anastomosis. Twenty-one patients (50%) with deep endometriosis benefited from laparoscopic excision of deep endometriosis nodules. The average age of patients was 34 years old. The laparotomy conversion rate was null. Following surgery, a significant improvement in dysmenorrhea, dyspareunia, chronic pelvic

pain, defecation pain, and lower abdominal pain was noted. In cases of deep endometriosis and colorectal resection, an improvement in the quality of life score assessed by the SF-36 questionnaire was observed. One patient (2.38%) refused the colorectal resection for objective reasons. The rate of postoperative complications was 2,38 % (a reintervention at 5 days postoperative for a ileostomial protection in a patient that underwent two intestine resections). The rate of hemoperitoneum, rectovaginal fistula, uroperitoneum and pelvic abscess was null. **Conclusions.** Laparoscopic segmental colorectal resection for endometriosis significantly improves the quality of life and the gynecological and digestive symptoms. However, women should be informed about the risk of complications, including rectovaginal fistula. The need for adherence to a national guide on the therapeutic conduct in deep endometriosis cases and the standardization of treatment allow us to achieve satisfactory results in terms of improving the quality of life in patients with colorectal resection. The preoperative investigations allow for surgical planning and the formation of a multidisciplinary team for the correct management and the complete excision of endometriotic lesions.

Keywords: minimally invasive surgery, laparoscopy, deep endometriosis, superficial endometriosis, rectosigmoid resection, endo-terminal mechanical anastomosis

Endometrial destruction techniques for heavy menstrual bleeding – systematic review *Tehnici de ablație endometrială utilizate în tratamentul menoragiei – review al literaturii*

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Endometrial ablation techniques continue to play an important role in the management of heavy menstrual bleeding. The techniques for endometrial ablation have evolved from the first-generation to the newer, second- and third-generation methods. The first-generation techniques are represented by endometrial laser ablation, transcervical resection of the endometrium, and rollerball endometrial ablation. The newer generation methods are: thermal balloon ablation, microwave endometrial ablation, hydrothermal ablation, bipolar radio-frequency endometrial ablation, and endometrial cryotherapy. The **aim** of this review is to compare the effectiveness, the safety, the acceptability, and the

complication rates of first-, second-, and third-generation methods available for endometrial ablation. **Conclusions.** All the techniques are effective and safe. Newer generation techniques are blind methods and can be performed rather under local anesthesia than general anesthesia. Second-generation techniques are associated with shorter operating times, and can be performed under local rather general anesthesia.

Keywords: endometrial resection, rollerball endometrial ablation, thermal ballon ablation, microwave endometrial ablation, hydrothermal ablation, bipolar radiofrecquency endometrial ablation, endometrial cryotherapy

Atypical uterine leiomyomatosis – case report

Leiomiomatoză uterină atipică – prezentare de caz

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Pelvic masses are a very common pathology among women and may involve gynecological or other non-gynecological organs. The most common tumor with gynecological implication is the leiomyoma. Intravascular leiomyomatosis (IVL) is a very rare entity, characterized by intravenous proliferation of benign smooth muscle cell tumor mass, which is not involving other tissues. Being such a rare pathology, the diagnosis is easily missed or delayed, thus IVL is considered to be an underestimated entity. Furthermore, in severe cases, it may cause noticeable complications, extending along the inferior vena cava, growing through the entire venous system, finally

reaching the heart and causing death. In addition to these complications, IVL is characterized by a high rate of recurrence. We present the case of a 44-year-old patient diagnosed with a voluminous uterine tumor who underwent hysterectomy followed by histopathological examination which revealed intravascular leiomyomatosis without any extrapelvic involvement. We also present a review of the international literature.

Keywords: leiomyoma, leiomyomatosis, intravascular, hysterectomy, myomatous erythrocytosis syndrome, hysterectomy

Sister Mary Joseph nodule. Moderately differentiated endometrioid endometrial carcinoma Nodul Sister Mary Joseph. Carcinom endometrial endometrioid mediu diferențiat

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A 82-year-old hypertensive female patient, obese, with one previous birth, with menopause at 47 years old, non-smoker, with a history of vaginal bleeding in January 2018, is sent by the dermatologist for an irregular umbilical tumor of 2/1 cm, recurrent at six weeks post-ablation, microscopically considered as a carcinomatous metastasis. Abdomino-pelvic MRI raises the suspicion of uterine carcinoma, which is confirmed by endometrial biopsy. It is done a extrafascial total hysterectomy with bilateral adnexectomy and pelvic nodes lymphadenectomy and ablation of a skin-adipose-conjunctive periumbilical tissue of 5/4 cm. There were no peritoneal metastases or other viscera abnormalities. The optic microscopy shows moderately differentiated endometrioid endometrial carcinoma, with areas of squamous differentiation, with invasion of the external myometrial half, without peritoneal invasion, with vessels metastatic embolizations, positive pelvic lymph nodes with moderately differentiated endometrioid endometrial carcinoma and desmoplastic reaction, and left ovary with mature teratoma. In the skin fragment, there is a neoplastic invasion of cribriform and tubular pattern, with areas of squamous differentiation, and vessels with neoplastic emboli. Sister Mary Joseph nodule was characterized by Hamilton Bailley (in 1949), after the initial description of William Mayo (1928), from the first observations of the assistant catholic nun Mary Joseph Dempsey at Saint Mary's Hospital, Rochester, Minnesota (USA). The medical literature associates the nodule to cancers with origin in the gastrointestinal and colonic tract, respiratory, urinary and genital tract - primary ovarian and endometrial cancers. The umbilical invasion may be due to the direct vessels' embolization by malignant endometrial cells, via the lymphatics which run along the obliterated umbilical vein, or via the remnant structures of the falciform and umbilical ligaments. Sister Mary Joseph nodule has a bad prognosis, the patient being under oncological monitoring, on chemoradiotherapy.

Keywords: cutaneous metastases, nodule, endometrioid endometrial carcinoma



A rare case of hereditary thrombophilia with heterozygous mutants of MTHFR and PAI-1 pregnancy-associated – case report and literature review

Formă rară de trombofilie congenitală prin mutante heterozigote de MTHFR și PAI-1 asociată sarcinii – caz clinic și revederea literaturii

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A 30-year-old pregnant women, nullipara, with two embryos death, former Yaz user (1 year), without antiphospholipid antibodies, with prophylactic cervical cerclage at 19 weeks of pregnancy, is readmitted in emergency at 21 weeks for heavy pelvic pain and abundant vaginal blood loss, with cerclage suppression. Under tocolysis and progesterone she presents three new episodes of intense pain and red, pulsatil blood loss from different cervical areas at 24-36 hours after admittance, with mechanical hemostasis by nylon sutures at the cervico-vaginal junction. The fourth episode is followed by severe anemia (Hb=6.03 mg/dL, Ht=18.32%), haemodinamic instability, coagulation disorders - hematomas, generalized petaechia, and at 24 hours after the last vaginal sutures she claims thoracic pain, dyspnoea and cyanosis. There are no registered fetal distress, placental abnormalities, cervical shortness below 2.5 cm, or maternal heart abnormalities at the ultrasound examination. It was not done the thoracic computed tomography because of the maternal refuse. After cardiologist consultation, it is appreciated a mild/moderate pulmonary thromboembolism, without deep legs venouos thrombosis, and continuous intravenous anticoagulant therapy is started – heparine 25.000 UI/day x 6 days, then fraxiparine in increased dosage continued to term, and during 6 weeks postpartum. The laboratory test confirmed the intravascular disseminated congulation with secondary fibrinolysis, being positive for heterozygous mutants of MTHFR (methylene tetrahydrofolate reductase deficiency C677T and A1298C), and PAI-1 (4G). The caesarean delivery is performed at 37 weeks for fetal distress at labor onset, with the extraction of a girl (3340 g, Apgar score=7/8), premature senescent placenta, thin umbilical cord, with a normal evolution of the mother and the baby postpartum.

Keywords: thrombophilia, cervico-vaginal thrombosis, pregnancy

Prematurity risk evaluation in HIV-positive patients Evaluarea riscului de prematuritate la pacienta HIV-pozitivă

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In Romania, at the end of 2018, there were 3685 HIV-positive women of fertile age (20-34 years old), the vast majority of whom were infected during the 1987-1990 period, so we are in front of another 10 years with an increased number of births from HIV-positive mothers. Several international studies have highlighted an increased incidence of premature and low birth weight in pregnancies with HIV-positive mothers, with risk factors such as viral load, low weight gain in pregnancy, maternal BMI, and duration of treatment. This paper contains an analysis of the data presented in the international specialty studies and their comparison with the data obtained from HIV-

positive patients whose pregnancies were followed-up at the "Prof. Dr. Panait Sîrbu" Clinical Hospital of Obstetrics and Gynecology, Bucharest, between 1 January and 31 December 2018. As a main conclusion, there is a discrepancy between the international studies and the experience of "Prof. Dr. Panait Sîrbu" Clinical Hospital of Obstetrics and Gynecology, by highlighting lower rates of premature or low weight for gestational age, the main factors being a better follow-up of the pregnancy and a better compliance with the treatment.

Keywords: HIV, pregnancy, prematurity, low weight for gestational age

Rhabdomyosarcoma of the cervix - case report

Rabdomiosarcom al colului uterin – case report

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Rhabdomyosarcoma is a malignant neoplasm which derives from embryonic muscle cells. In children, it is the most commonly discovered soft tissue tumor, whereas in adults rhabdomyosarcomas are rare, representing less than 5% of soft tissue tumors and less than 1% of all malignant cancers. The neoplasm has a tropicity for the head and neck area, lymph nodes, genitourinary tract, and the retroperitoneum. The surgical treatment for cervical rhabdomyosarcoma can be conservative or radical surgery, with survival rates of vaginal and cervical lesions reported to be of 96% and 60%, respectively. We present the case of a 46-year-old woman who addressed the clinic in mid 2017 due to an abnormal vaginal discharge. The gynecologic examination revealed a large 5/6 cm cervical mass with grape-like feature protruding into the vagina. A biopsy – local resection – was performed. The

final pathologic result was consistent with embryonal type rhabdomyosarcoma. The diagnosis was explained to the patient and a plan of treatment was issued, but she refused any further investigations or treatment. She has since came back two times with recurrence of the mass, each time refusing the radical surgery or any other type of treatment, only local resection being done each time. This case reminds that embryonal rhabdomyosarcoma can be found in uncommon sites, not only during childhood, but also in older females, and an exophytic cervical mass, of polypoid shape and grey colour, is best to be biopsied. Longer follow-up is required because of the lack of data on recurrence and survival rate, especially when only local resection is performed.

Keywords: rhabdomyosarcoma, cervix, surgical management

The importance of microsatellite instability in endometrial cancer Importanța instabilității microsatelite în cancerul de endometru

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Endometrial cancer is one of the most common cancers, with an incidence of 8 per 100,000 women. In Europe, endometrial cancer is ranked 4th as frequency and 10th for mortality due to cancer. Microsatellite instability (MSI) is an important factor in the carcinogenesis of various organs or systems. Clinical-pathological and molecular characteristics of high molecular instability phenotypes have been extensively studied for colorectal and gastric cancers. However, the clinical-pathological impact of MSI on endometrial carcinomas is not

well known. It is currently estimated that 25-45% of endometrial carcinomas exhibit microsatellite instability. This paper aims to present a review of the recent international literature focusing on the association between microsatellite instability and clinical-pathological features of endometrial cancer. At the same time, the management and prognosis in case of microsatellite instability will be reviewed.

Keywords: endometrial cancer, microsatellite instability, anatomopathology

Varicella-zoster virus infection in pregnancy – management protocol

Infecția cu virus varicelo-zosterian în sarcină – protocol de management

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Varicella-zoster virus (VZV) is a DNA virus. It is highly contagious, the virus spreading from person to person through air drops and direct contact. The incubation period of the infection is 10-14 days. The incidence of infection in pregnancy is 1-5 cases per 10,000 pregnancies, but lately, due to the antivaccine trend, an increase has been noticed. The congenital varicella infection, the maternal pneumonia due to varicella-zoster virus and the neonatal VZV infection are highly associated with fetal-maternal morbidity and even mortality. This paper aims at presenting a protocol for the management of varicella-zoster infection in pregnancy based on recent international studies

and protocols. The main recommendation is immunological status screening and pre-pregnancy vaccination of all non-immune women, as vaccination during pregnancy is not recommended. In the first 96 hours of exposure of pregnant women to varicella, it is possible to administer immunoglobulin. If the infection develops during pregnancy, it is necessary to explain to the patient the maternal and fetal risks. A detailed ultrasound scan is necessary to highlight possible fetal damage. The treatment of infection in pregnancy is done with acyclovir, given orally or intravenously, depending on the degree of infection.

Keywords: varicella, zoster, VZV, pregnancy



Type 1, type 2 and gestational diabetes mellitus impact on the placental structure

Impactul diabetului de tip 1, de tip 2 și gestațional asupra structurii placentare

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Diabetes is the most common medical complication associated with pregnancy. During pregnancy complicated with maternal diabetes (DM), the placenta suffers certain pathological, functional and structural changes. DM was correlated with a rapid progressive microangiopathy and this, in turn, may be associated with capillary hypertension and changes in capillary permeability. The objective of the study is to identify the clinical correlations with influence on gestation in general, and on the placental structure in particular, in pregnancy associated with type 1 (T₁DM), type 2 (T₂DM) and gestational diabetes mellitus (GDM). The impact of the clinical conditions associated with DM on placenta has been analyzed and correlated with the ultrasound (US), morphological, histological and immunohistochemical study of the placental structure. Preexisting maternal hypertension, preeclampsia and obesity were the main associated conditions. The US examination of placental characteristics revealed an increase in placental thickness in the second trimester. The macroscopic analysis showed that the placentas of women with diabetes are heavier. Gross pathological analysis of maternal and fetal surfaces of placentas revealed subcortical or basal plaque fibrin deposition, and placental infarction or intervillous thrombosis. From the microscopic point of view, the findings include fibrinoid necrosis, intervillous fibrosis, focal hyaline degeneration, villous immaturity, chorangiosis, placental calcifications, placental infarction or decidual vasculopathy. Maternal hypertensive disorders amplify the spectrum of morphological changes in the placenta. Placental immaturity and villous capillary dysfunction are characterized by increased angiogenesis and enhanced vascular permeability. The diabetic placenta does not show specific changes, but different associations may be a diabetic pathological pattern influenced by associated conditions, especially preeclampsia, obesity, dyslipidemias and the lack of euglycemia during pregnancy.

Keywords: morphology, immunohistochemistry, ultrasonography, glycemic control, diabetic pattern

Cancer and pregnancy

Neoplaziile și sarcina

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The diagnosis of cancer during pregnancy is a challenge for the clinician, pregnant woman and her fetus. In several studies, the term "gestational cancer" includes not only the cancer diagnosed during pregnancy, but also in the first year postpartum. Some studies reported an incidence of pregnancy-related cancer from 0.02% to 0.1%, with lower rates in developing countries due to low birth weight. Breast cancer affects about 1 in 3000 pregnant women, and is considered the second malignancy in pregnancy. Cervical cancer is the most common gynecological malignancy during pregnancy. The incidence rates range from 0.1 to 12 per 10,000 pregnancies. For cervical intraepithelial

neoplasia (CIN), the reported incidence rates range from 1.30 to 2.7 per 1000 pregnancies. Cervical cancer screening is an essential component of prenatal care. The diagnosis and the management of intraepithelial cervical neoplasia (CIN) during pregnancy are provocative, and there is insufficient information to allow a definitive evidence-based approach. A multidisciplinary approach is essential; the management strategies should include maintaining the quality of life during the current pregnancy and preserving fertility.

Keywords: pregnancy, breast cancer, cervical cancer, screening, chemotherapy, radiotherapy

The importance of mismatch repair deficiency detection in endometrial carcinoma

Importanța detectării deficienței de reparare mismatch în carcinomul endometrial

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Endometrial carcinoma is a neoplasia with increased incidence worldwide, affecting women of different ages. The studies focused on the carcinogenesis of endometrial carcinoma have identified a similar pattern with colorectal carcinomas. We studied the relationships between age, histological pattern and MMR classes. Mismatch repair deficiency was assessed by immunoreactions for MSH2, MLH1, MSH6 and PMS2, classify-

ing tumours into four MMR classes (normal, epigenetic defect, probable mutation, and MSI-low). The nuclear immunoreactions were carefully identified and compared with internal positive control. Mismatch repair deficiency detection is a useful screening marker, as well as a prognostic factor.

Keywords: carcinogenesis, DNA, mismatch repair, endometrial carcinoma

Why do we sometimes need immunohistochemistry in the diagnosis of mesenchymal uterine tumors? De ce avem nevoie de teste suplimentare de imunohistochimie în diagnosticul tumorilor mezenchimale uterine?

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Mesenchymal tumors of the uterus represent a high number of routine practice in gynecological pathology, and the pathology is heterogenous, with diagnostic challenges. There is a large variation in clinical, pathological and prognostic patterns of these entities, smooth muscle and endometrial stromal constituting the majority of the group. Although histopathological slides are the gold standard and sometimes enough for the diagnosis of mesenchymal uterine tumours,

difficult cases need ancillary tests. A large panel of immunohistochemical antibodies provides more information. We present the algorithm used for the differential diagnosis between uterine smooth muscle tumors, endometrial stromal tumors, UTROSCTs, PEComas, and the most frequently used imunohistochemical markers.

Keywords: immunohistochemistry, uterine smooth muscle tumors, endometrial stromal tumors, UTROSCTs, PEComas

New values and new approaches in 2019 – hypertension and menopause Noi standarde și abordări în 2019 – hipertensiunea arterială și menopauza

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High blood pressure should be treated at 130/80 mm Hg rather than 140/90, according to the first comprehensive new high blood pressure guidelines in more than a decade. The guidelines have been released by the American Heart Association (AHA) and the American College of Cardiology (ACC) for the detection, prevention, management and treatment of high blood pressure. The guidelines were presented at the association's 2017 Scientific Sessions conference in Anaheim, the premier global cardiovascular science meeting for the exchange of the latest advances in cardiovascular science for researchers and clinicians. The new guidelines stress

the importance of using proper techniques to measure blood pressure. Blood pressure levels should be based on an average of two to three readings on at least two different occasions, according to medical experts. At the age of menopause, the main risk is represented by cardiovascular diseases, and high blood pressure accounts for the second largest number of preventable heart disease and stroke deaths, second only to smoking. It is commonly known as the "silent killer", because often there are no symptoms, despite its role in significantly increasing the risk of heart disease and stroke.

Keywords: hypertension, menopause, heart disease



Prenatal care for pregestational diabetes mellitus

Tinte terapeutice prenatale pentru diabetul zaharat preexistent

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It is still a debate which is the best combination of early predictive markers. Large-scale observational studies showed that simple, well known and easy to achieve parameters as maternal age, blood pressure and body mass index (BMI) could be used with good sensitivity and specificity, and in the presence of pregestational diabetes mellitus their predictive values are increased. The evaluation of maternal BMI, ethnicity and medical history in a population of nulliparous women could detect 55% of women with early-onset preeclampsia, with a 90% specificity. Using some other serum biomarkers together with demographic data improved the detection rate of preeclampsia to 75%. The Doppler measurement on the uterine artery resistance is a further value associated with increased risk for IUGR (in utero growth restriction) and preeclampsia. In this context it becomes debatable if other first-trimester or early second-trimester markers, which showed up a value in preeclampsia and IUGR prediction, should be included in the formula for preeclampsia risk, because of the costs and small added values in terms of specificity and sensibility for the general screening. However, the answer will need validation of the performance and benefits of the use of these markers in large cohort studies and appropriate cost-effectiveness analyses. On the other hand, preexisting diabetes mellitus as a risk status for pregnancy complications, the value of the pregnancy, and a rather low number of pregnancies might become appropriate to make these high-cost measurements to improve the detection rate, or may be even to decide an early intervention to all the pregnancies after evaluating the risk-benefit approach. With the discovery of biomarkers and the technological advances, new combinations of predictors will emerge in the near future to improve the detection rates and specificity.

Keywords: pregestational diabetes mellitus, prenatal care, pregnancy complication

Morphogenetic correlations of increased nuchal translucency in fetuses with normal first-trimester scan

Corelații morfogenetice ale translucenței nucale crescute la feții cu morfologie normală în primul trimestru

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Introduction. Increased nuchal translucency (NT) at a gestational age of 11-14 weeks frequently represents the fenotipical expression of some chromosomal anomalies. Moreover, many of these syndromes associate morphological anomalies, especially in the context of an increased NT. First-trimester ultrasound scan remains the basis of prenatal care, and one of the objectives is represented by the major fetal anomalies detection. The purpose of this study is to evaluate the significance of an increased NT in fetuses with normal first-trimester morphology. Materials and method. We did a retrospective study in the Prenatal Diagnosis Center of the Emergency County Hospital of Craiova and at MEDGIN Craiova. In this study we included cases which presented for a first-trimester ultrasound genetic screening, where a detailed morphological examination protocol was followed. The patients who presented fetuses with a NT of over 3 mm underwent an invasive maneuver - chorionic villus sampling (CVS) or amniocentesis. The genetic counseling was performed prior to the maneuver. **Results.** Over the course of two years, 527 patients were examined, and 5% of them presented a NT of more than 3 mm. In more than 50% of these cases, an increased NT represented an isolated ultrasound marker, without any other associations, and the genetic test results were normal. In cases where increased NT and structural anomalies were present, major genetic and morphological modifications were diagnosed, with an absolute indication for the therapeutic termination of the pregnancy. **Conclusions.** Increased NT without any other morphological anomalies in the first-trimester ultrasound scan is associated in the majority of the cases with normal fetus karyotype and normal fetus prognosis on short and medium term (birth). However, a detailed morphological evaluation at the end of the first trimester is required in these situations, performed in a specialised center.

Keywords: nuchal translucency, malformations, ultrasound morphology

Thyroid nodules in a young patient trying to conceive

Noduli tiroidieni la o pacientă tânără care dorește sarcina

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Introduction. Up to 50-70% of the population (women seem more affected than men) have a thyroid nodule (TN) of various dimensions, especially less than 1 cm. The incidence is age-related, but the prevalence is also consistent in women of reproductive age. The investigations in order to conceive usually involve the thyroid panel and the accidental ultrasound detection of a TN is a relatively frequent scenario. The relationship with low fertility rate is less strong, with the exception of autoimmune thyroid background. Aim. To introduce a series of cases with TN detected during investigations for fertility. **Method.** These are two case reports. The hormonal and imagery profile is provided. **Case 1.** We present the case of a 26-year-old non-smoking female coming from a nonendemic area. She is nulipara. The personal and family medical history is irrelevant. She has regular menses and seeks for fertility. The gynecological exam is normal, so she was referred for endocrine assays. The thyroid blood tests showed normal TSH (1.3 µUI/mL), calcitonin (4.3 pg/ mL; N: 1-4.8 pg/mL) and TPO antibodies (10 UI/mL; N<35 UI/mL). Thyroid ultrasound shows right lobe of 4.9/2.1/2.1 cm, and left lobe of 4.6/1.7/1.4 cm. The right lobe is displayed by a hypoechoic TN (peripheral halo, vascularised) of 2.1/1.5/3.2 cm, with another of 0.7/0.4/0.4 cm, without lymph nodes involvement. Due to high dimensions and ultrasound features, the patient was referred for surgery. Case **2.** A 34-year-old smoking female, coming from a nonendemic area, was admitted for fertility issues. She has four healthy children (the oldest 8 years ago), with the same partner. She presents irregular menses for the last five months. TPOAb are positive (270 UI/mL), with a normal thyroid function (TSH = $2.3 \mu UI/mL$; N: $0.5-4.5 \mu UI/mL$). The thyroid ultrasound pattern is hypoechoic, with a few TN of maximum 0.3 cm. The clinical examination accidentally revealed lipomas at the skull of 2 cm (confirmed at computed tomography). The lipid profile was normal, unrelated to thyroid and skull anomalies. **Conclusions.** Both cases had thyroid anomalies most probably unrelated to fertility issues.

Keywords: thyroid, nodule, ultrasound

Diabetes mellitus and pregnancy

Diabetul zaharat în sarcină

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Gestational diabetes represents a diabetes diagnosed during pregnancy, in the second or third trimester, which is not type 1 diabetes or preexisting type 2 diabetes. Diabetes diagnosed in the first trimester of pregnancy is defined as preexisting diabetes. The prevalence of diabetes in pregnancy is steadily increasing in the USA, most of which are gestational diabetes (approximately 90% of cases). The other types of diabetes in pregnancy are type 1 and type 2 diabetes mellitus. Preexisting type 2 diabetes mellitus represents approximately 8% of all types of diabetes in pregnancy. The increase in the prevalence of gestational diabetes occurred in parallel with the increase in the prevalence of obesity. **Materials and method.** Type 1 diabetes mellitus and preexisting type 2 diabetes mellitus are associated with a greater risk of maternal and fetal complications than gestational diabetes. Among the most common complications are spontaneous abortion, fetal anomalies (anencephaly, microcephaly, congenital heart disease, caudal regression), macrosomia, neonatal hypoglycemia, neonatal hyperbilirubinaemia, and others. The diagnosis of gestational

diabetes is performed with either one-step or two-step strategy in pregnant women between 24 and 28 weeks of gestation. Diabetes screening is also recommended at the first prenatal visit for women with risk factors for diabetes. Also, gestational diabetes has been associated with an increase in the risk of developing maternal type 2 diabetes, as high as 50-70% after 15-25 years. Therefore, there is recommended to test the women with gestational diabetes, between 4-12 weeks postpartum, using the oral glucose tolerance test (OGTT). If it is normal, the test should be performed every one to three years. **Conclusions.** The management of diabetes in pregnancy involves nutritional medical therapy and/or pharmacological treatment, in order to obtain glycemic targets that have been associated with the lowest risk of maternal and fetal complications. Considering the possibility of diabetes' complications (retinopathy) during pregnancy, it is also necessary to screen for them in women with preexisting diabetes.

Keywords: gestational diabetes, diabetes complications, glycemic targets



Factors influencing the pacient in choosing a contraceptive method

Factorii care influențează alegerea de către pacientă a metodei contraceptive

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Introduction. Nowadays, the multitude of contraceptive methods allows the individualization of the contraceptive treatment according to the needs and wishes of the patient. **Materials and method.** We performed a retrospective study at the "Prof. Dr. Panait Sîrbu" Clinical Hospital of Obstetrics and Gynecology, Bucharest, Family Planning Center, analyzing the factors influencing the patients when requesting the starting of contraception. We analyzed the recommended and the chosen contraceptive method, the availability of the method, and the associated pathology. The patients were divided into three lots, corresponding to three particular chronological periods. Lot A: 2004-2005, when the National Contraceptive Program offered seven free contraceptive methods to large patient groups. Lot B: 2013-2014, a period during which a certain type of oral contraceptive was temporarily withdrawn from marketing. Lot C: a period without any free contraceptive method available. **Results.** In group A, 93% of patients chose the recommended contraceptive method and 78% of them with no additional costs. In group B, 56% of patients chose the recommended contraceptive method, 88% of them refusing to take oral contraceptives. In group C, 80% of patients chose the recommended contraceptive method, and 56% of those who opted for another contraceptive method invoked financial issues. **Conclusions.** In all these groups, the factors that influenced the choice of the contraceptive method varied over time. In lot A, the medical recommendation was decisive, in lot B the choice of the contraception was made under the influence of the strong negative mediatizations of a certain contraceptive method, and in lot C the lack of free contraceptive methods influenced the patient's decision.

Keywords: contraceptive methods, starting contraception, availability of treatment

Restless legs syndrome in pregnancy – pathophysiological aspects and management Sindromul picioarelor neliniştite în sarcină – aspecte fiziopatologice și conduită terapeutică

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Restless legs syndrome (Willis-Ekbom disease), characterized by the urgent need for leg movement during rest periods, has a significantly increased incidence during gestational period, being three times more frequent in pregnancy compared to the general population. Approximately one in five women will experience symptoms typical for this syndrome during pregnancy, especially during the last trimester. In terms of pregnancy prognosis, restless legs syndrome has been associated with an increased incidence of gestational hypertension, preeclampsia, depressive disorder, chronic fetal distress, intrauterine growth restriction, prematurity, and caesarean delivery. Poor nighttime sleep quality associated with marked sleepiness, physical and psychic inefficiency throughout the day are the main factors leading to therapeutic behavior requirement. The main

etiological factors involved are genetic predisposition, iron and folate deficiency, elevated estrogen levels and nerve compression. Although treatment differs depending on symptoms severity and associated conditions, the first line of therapeutic approach includes iron supplementation, physiotherapy and psychotherapy. In case of severe, refractory symptomatology significantly impacting the quality of life, the allowed treatment includes the minimum effective dose of clonazepam (0.25 mg/day) and carbidopa-levodopa (25/100 mg). For extreme cases, refractory to the aforementioned medication, oxycodone therapy may be considered also at the lowest dose. In spite of the transient appearance of the restless legs syndrome during pregnancy, these cases require specific monitoring due to possible associated conditions.

Keywords: restless legs, pregnancy, treatment

Monitoring and management of pregnancies complicated with fetal heart arrhythmias Monitorizarea și managementul sarcinilor complicate cu aritmie cardiacă fetală

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With a relatively frequent incidence of 1-2%, fetal heart arrhythmias may represent a sign of compromised fetal status. Most arrhythmias are isolated, but in some cases they are associated with structural or functional cardiac abnormalities. A series of specific investigations, such as the detection of anti-Ro/SSA and La/SSB autoantibodies in lupus patients, may indicate the etiology. Detailed echocardiography, specialized echocardiography and cardiotocographic monitoring can direct the management towards expectative or further fetal cardiology consult. Fetal arrhythmias with irregular rhythm, translating intermittently blocked beats, have good prognosis, are well tolerated and can rarely progress to significant cardiac pathology. Thus, the presence of 3-5 extrasystoles per minute with normal heart rate requires high-level fetal heart echocardiography and weekly monitoring of heart rate.

Tachycardia or bradycardia associated with fetal cardiac extrasystoles have indication for specialized fetal cardiac evaluation based on detailed echocardiography and weekly cardiotocographic monitoring, along with rigorous fetal movement monitoring by the mother. Fetal sinus tachycardia can be considered normal if it occurs sporadically during fetal movements. The indication of transplacental treatment occurs in case of fetal hydrops or persistent tachycardia (>220 beats/min), digoxin being the reference drug. Fetal bradycardia frequently associates a background cardiac pathology, heterotaxia or long QT syndrome. The presence of fetal heart arrhythmias is not an absolute indication of birth by caesarean section if there is the possibility of continuous fetal monitoring, otherwise it is the best option.

Keywords: management, fetal arrhythmia, echocardiography

Abdominal cerclage *Cerclajul abdominal*

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The abdominal cerclage is a therapeutic procedure that performs a reliable cervical canal obliteration in specific selected cases. The abdominal cerclage is indicated for cervico-isthmic incompetence in patients who had repeatedly failed transvaginal cerclage, and also in those with anatomical abnormalities represented by a very short or absent cervix due to congenital or surgical conditions. The paper aims to present a series of eight cases in which abdominal cerclage was performed. The abdominal cerclage can be performed through open abdominal route or laparoscopic. The procedure can be practiced prophylactically before conception or during pregnancy, in the first trimester of gestation either prophylactically, or as an emergency solution for imminent abortion. The abdomi-

nal cerclage is a safe procedure, with an excellent fetal outcome, and is an alternative treatment for cervico-isthmic incompetence. The advantages of the abdominal cerclage are represented by the placement of the cerclage tape in close proximity of the internal os, the absence of a foreign body in the vagina (that could cause infection), decreased risk of suture migration, and the ability to keep the suture in place for future pregnancies. The abdominal cerclage is the only therapeutic solution in patients with a history of recurrent abortions resulting from failed transvaginal cerclages, as well as in patients with very short or absent cervix.

Keywords: abdominal cerclage, cervico-isthmic incompetence, recurrent abortions

Laparoscopic tubal reanastomosis outcomes Rezultatele reanastomozei tubare laparoscopice

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Background. Encountered among methods of contraception, tubal sterilization is not a priority in Romania. The aim of this study is to present the reproductive outcome reported in Filantropia Clinical Hospital of Obstetrics and Gynecology after laparoscopic tubal reanastomosis. **Case reports.** We present two cases which underwent laparoscopic reversal. The first case opted for reversal tubal ligation after 7 years from her single caesarean section. Despite the unilateral recanalization achieved, the woman conceived after only 6 months. The

second case was more challenging, taking into consideration the patient's medical history. Despite both tubes being permeable at the end of the procedure, the patient did not conceive at that time. **Conclusions.** Our experience confirms that the main factors that can predict the success of tubal reanastomosis are the maternal age at the time of the reversal and the remaining length of the tube after recanalization.

Keywords: laparoscopic tubal reanastomosis, tubal ligation, tubal recanalization



Laparoscopic myomectomy in young women

Miomectomia laparoscopică la pacientele tinere

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Uterine leiomyoma represents the most common benign tumour in women of reproductive age, with a prevalence of 20-50%. Most women are asymptomatic, but 30% of them report metrorrhagia, pelvic pain, dyspareunia, urinary and bowel symptoms or infertility. Symptomatic fibromas and the desire for childbearing are the most common indications for myomectomy. Some patients are candidates for laparoscopic myomectomy. Our study presents a series of case re-

ports, surgical images, controverses and literature reviews. Laparoscopic myomectomy has numerous advantages than classical myomectomy, such as lower blood loss, reduced hospitalization, low overall morbidity and less postoperative pain. The rate of postoperative adhesions is lower for laparoscopic myomectomy.

Keywords: myomectomy, uterine fibromas, laparoscopic myomectomy

Vitamin A supplementation during pregnancy Vitamina A în sarcină

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Vitamin A is an essential nutrient that plays a major role in the prevention of anemia and cell growth, and also in fetal development and in supporting metabolism during pregnancy. The main sources of vitamin A are carrots, broccoli, spinach, sweet potatoes, liver, eggs and milk. According to the American Pregnancy Association, the recommended daily allowance (RDA) of vitamin A for healthy women during pregnancy is 770 mcg/dl. Most studies have shown an association between high doses of preformed vitamin supplements and congenital birth defects in pregnant women. Birth defects described include malformations of the heart, lungs, eyes and skull. The risk of birth defects has been correlated with a preformed vitamin A consumption greater than 10000 IU/day, while doses of preformed vitamin A from supplements below 3000 mcg/day (10000 IU/day) showed no increase

in the risk of birth defects. Furthermore, in women with vitamin A deficiency, some studies have shown that low-dose vitamin A consumption may be protective against birth defects. Also, there is no correlation between vitamin A from beta-carotene and the risk of birth defects. On the other hand, vitamin A deficiency leads to other problems, such as xerophthalmia, anemia, lowered immunity system during pregnancy and lactation, and even slower growth and development in children. In conclusion, vitamin A supplementation should only be recommended for pregnant women in areas where vitamin A deficiency is endemic. So, the focus should be on a diet that can provide the variety of nutrients needed in pregnancy.

Keywords: preformed vitamin A, supplements, birth defects, fetal development, high doses, diet

Velamentous cord insertion – importance of diagnostic assessment Inserția velamentoasă de cordon ombilical – importanța diagnosticului

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The normally insertion of the umbilical cord is directly into the central part of the placenta, providing oxygen and nutrition for the fetus. Velamentous cord insertion is an abnormal insertion of the umbilical cord, in which the umbilical vessels insert into and course through the amniotic membranes before reaching the placental mass. It has been more commonly associated with placenta praevia than with normally located placentas. Velamentous cord insertion may be prenatally detected on ultrasound examination. The criteria for ultrasound diagnosis are: the umbilical vessels diverging as they traverse the membrane, entering the placenta margin parallel to the uterine wall and connecting to the subchorionic vasculature. The cord insertion remains immobile even when the uterus is shaken. The use of color Doppler enhances the identification of the vessels, but a definitive diagnosis is made by gross examination of the placenta, membranes and cord, after delivery. Velamentous cord insertion has been correlated with some adverse perinatal outcomes, including caesarean delivery, preterm delivery, fetal growth restriction, placental abruption and low Apgar scores. All of these outcomes are likely secondary to a lack of protective Wharton jelly surrounding the fetal vessels, which are proned to compression, kinking and rupture during labor, leading to fetal heart rate abnormalities and even to fetal death. Kinking and compression are also correlated with thrombosis of the vessels, which leads to placental infarction, neonatal purpura and even amputation of fetal limbs or digits. Fetal death and exsanguination may occur when the rupture of the fetal membranes leads to the rupture of the vessels, which are attached to the chorion and the membranous vessels are typically close to or cover the cervix (vasa praevia). In conclusion, prenatal diagnosis of the velamentous cord insertion plays a critical role in the prevention of the fetal death and adverse perinatal outcomes.

Keywords: velamentous cord insertion, *vasa praevia*, ultrasound examination, caesarean delivery, preterm delivery, fetal death, fetal growth restriction, placental infarction

Laparoscopic myomectomy of large and multiple myomas – our experience

Miomectomia laparoscopică pentru mioame multiple voluminoase – experiența noastră

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Introduction. Laparoscopic myomectomy offers the possibility of a minimally invasive approach to treat large and medium sized (<12 cm) subserous and intramural multiple myomas, reducing the risk of perioperative complications. Infertility has been linked with the appearance of uterine myomas. It is said that the laparoscopic approach of the myomas can improve fertility rates. In this paper, we detail our experience in laparoscopic myomectomy of large and multiple myomas and demonstrate improved fertility rates. Materials and method. A total of 145 patients were operated during the study period, between May 2012 and August 2018. The patients' age was between 20 and 45 years old, and the indications were: meno-metrorrhagia, pain, pressure, infertility, recurrent abortion, size or rapid growth, or urinary symptoms. All patients who were included in this study had more or at least two

myomas. **Fertility results.** In our 91 patients known with infertility, after laparoscopic myomectomy the rate of patients achieving pregnancy was 53.1% (43 patients). The 43 patients obtained 51 pregnancies. In patients in whom the only factor for infertility was the presence of myomas, the rate of achieving a pregnancy was 70% (17 patients), which is very encouraging, comparing to the group that had several other infertility factors, with a rate of 43% (23 patients). We didn't report any uterine rupture. **Conclusions.** The use of laparoscopic surgery can reduce the hemorrhagic risk associated with laparotomy, improves the rate of obtaining a pregnancy, and preserves fertility. The small myomas must also be ablated because of the risk of growing afterwards.

Keywords: laparoscopy, leiomyomas, myomectomy, fertility, pregnancy, surgical outcomes

Laparoscopic approach of mature cystic teratoma

Abordul laparoscopic în tratamentul teratomului ovarian matur

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Introduction. Ovarian mature cystic teratomas are commonly encountered in young women of reproductive age, accounting for up to 60% of benign ovarian masses and often present both diagnostic and management dilemmas. Infertility has been linked with the appearance of dermoid cysts. So far, various approaches and procedures were employed in surgical practices. In this work, we detail our experience in laparoscopic cystectomy of large and multiple ovarian teratomas and demonstrate improved fertility rates. **Materials and method.** A total of 35 patients were operated during the study period, between April 2015 and July 2018. The patients' age was between 20 and 45 years old, and the indications were: pain in the lower abdomen, pressure, infertility, rapid growth or urinary symptoms. All patients who were included in this study had been diagnosed with transvaginal ultrasound scan. Fertility results. In our 20 patients known with infertility, after laparoscopic cystectomy the rate of patients achieving pregnancy was 60% (12 patients). The 12 patients obtained 15 pregnancies. We report that contents spillage occurred in seven patients (20%) and it was particularly associated with larger cysts. All cases were concluded laparoscopically, we didn't convert any case to laparotomy. So far, we haven't reported any recurrence after laparoscopic ovarian cystectomy. **Conclusions.** Although some investigators recommended for mature cystic teratoma >10 cm the laparotomic approach, we consider the laparoscopic approach as the gold standard for the management, including for very large cysts. The risk of chemical peritonitis after contents spillage is extremely rare, and can be certainly overcomed with thorough peritoneal lavage, using large quantities of warmed fluid.

Keywords: laparoscopy, ovarian teratomas, cystectomy, fertility, surgical outcomes



Clinical, morphological and immunohistochemical study of adenomyosis

Studiu clinic, morfologic și imunohistochimic al adenomiozei

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Introduction. Adenomyosis is a benign pathology defined by the presence of endometrial glands in the miometrium, accompanied by chronic pelvic pain, infertility and vaginal bleeding. It is a hormonal dependent condition and is common in reproductive age. Adenomyosis areas differ from the normal endometrium by increased local production of estrogen or prostaglandins and resistance to progesterone action. **Materials and method.** The study included 23 patients, aged 26-52 years old, diagnosed with adenomyosis. Postoperatively obtained specimens were included in paraffin and studied histologically and immunohistochemically. The blocks were cut by the microtome, the sections were applied on simple slides for histological staining of Hematoxylin-Eosin and on Poly-L-lysin slides for the immunohistochemical stains. The antibodies were: anti-estrogen receptors (ER), anti-progesterone receptors (PR), anti-

cytokeratin 7 (CK7), anti-cytokeratin 20 (CK20). **Results.** Classical Hematoxylin-Eosin staining showed the presence of mono-layered, cylindrical glandular epithelial tissue in the structure of the myometrium, and with immunohistochemistry we showed that these glands were of endometrial origin, being CK7-positive and negative at CK20, making a differential diagnosis with an eventual metastasis from the digestive tract. The receptors for estrogen and progesterone are present in the structure of these glands. **Conclusions.** Adenomyosis is a benign pathology diagnosed with certainty by histopathological examination. Receptors for estrogen and progesterone are features for endometrial tissue, and cytokeratins make the differential diagnosis with digestive epithelium.

Keywords: adenomyosis, pain, infertility, histology, immunohistochemistry

Ethanol sclerotherapy of an ovarian endometrioma

Alcoolizarea chistului endometriozic

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Endometriosis is a complex gynecological pathology, affecting between 6% and 10% of reproductive-age women. Endometriomas are ovarian cysts that are found in 17-44% of the women with endometriosis. The major two problems regarding this disease are pain and infertility. The conventional treatment of this pathology is laparoscopic surgery. Unfortunately, some patients need more than one surgery, due to some reasons: an incomplete initial procedure, recurrence or excision of new lesions. The greatest disadvantage

of the surgical technique is the fact that, most of the times, it diminishes the ovarian reserve. In order to avoid this, a conservative treatment has been advocated. A new promising technique, that preserves ovarian reserve and lowers the recurrence rate, is sclerotherapy of the endometrioma. It consists of ultrasound-guided vaginal cyst aspiration and injecting 95% ethanol into the cyst cavity.

Keywords: endometrioma, poor ovarian reserve, recurrence, sclerotherapy, ethanol 95%

Angiogenic biomarkers for the prediction of preeclampsia

Potențiali biomarkeri angiogenici pentru predicția preeclampsiei

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Preeclampsia (PE) is one of the main causes of maternal and neonatal morbidity and mortality worldwide. Current PE definitions are unsatisfactory in estimating the negative pathology outcomes. Preeclampsia is primarily a vascular disease, especially of the endothelium, and its pathology is thought to be due to placental hypoperfusion, hypoxia, oxidative stress and inflammation. An imbalance of proangiogenic and anti-angiogenic factors in the maternal circulation has been demonstrated during preeclampsia, specifically elevated levels of fms-like anti-angiogenic (sFlt-1) soluble tyrosine kinase and reduced growth fac-

tor pro-angiogenic placenta (PIGF). Estimating the sFlt-1/PIGF ratio allows the identification of women at high risk of imminent birth and maternal and neonatal unfavorable development. The diagnostic and prediction value of the sFlt1/PIGF ratio in patients at risk for placental-related disorders – namely, PE, HELLP, IUGR and dead fetus – has been demonstrated in recent literature, and the estimation of sFlt1/PIGF become an additional tool in managing these disorders, especially PE.

Keywords: preeclampsia, pregnancy, angiogenic biomarkers, anti-angiogenic biomarkers, IUGR

Rare case of umbilical cord hematoma in a term neonate

Caz rar de hematom de cordon ombilical la un nou-născut la termen

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We present a rare case of postpartum umbilical cord hematoma with unknown cause in a term newborn. The neonate was born by caesarean section indicated for failure of medical induction of labour in a 28-year-old primipara with a 41-week pregnancy. The mother did not suffer from any pathology throughout gestation, presenting a morphologically normal foetus and negative urine and cervical cultures. She delivered a 3690-gram male newborn, with an Apgar score of 9 at one minute and 10 at five minutes, following an uncomplicated caesarean section. The newborn presented good postnatal adaptation, and breast alimentation was initiated in the first day of life. The C-reactive protein (CRP) of the newborn was negative and his evolution was favourable in the first two days of life. In the third day of life, the neonate presented swelling of the umbilical cord stump, with a dark-red coloration, suggestive for hematoma. Antibiotic prophylaxis and local antiseptic therapy were initiated, CRP was repeated and bacteriological samples were collected, the results being negative. After two days of local antiseptic treatment, the umbilical stump fell and the umbilicus presented normal appearance. The evolution of the neonate was good, and he was discharged in the fifth day of life. The mother did not present any sign of infection or thrombosis, with a physiological recovery. The particularity of the case is represented by the rarity of the pathology, until present only a few cases of umbilical cord haematoma being described in the specialty literature. The etiology in this case is idiopathic, the infectious, malformative, thromboembolic and mechanical causes being ruled out. The only risk factor in our case could be represented by the advanced gestational age (41 weeks of pregnancy), which could explain partially the frailty of the umbilical cord vessels.

Keywords: umbilical cord, hematoma, rare neonatal complication