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SUMMARIES OF "VASILE DOBROVICI" MEDICAL DAYS NATIONAL CONFERENCE

• 5-7 May 2022, Iași, Romania •

SUMMARIES OF THE 4TH NATIONAL CONGRESS OF THE EAST-EUROPEAN SOCIETY OF ENDOMETRIOSIS AND INFERTILITY

and THE 7TH NATIONAL CONFERENCE OF THE ROMANIAN SOCIETY OF HPV

• 2-4 iunie 2022, Eforie Nord, Romania •

Societatea Română de Obstetrică și Ginecologie



Societatea Română de Ultrasonografie în Obstetrică și Ginecologie



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Societatea de Uroginecologie din România



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SUMMARIES OF “VASILE DOBROVICI” MEDICAL DAYS
NATIONAL CONFERENCE,
5-7 MAY 2022, IAȘI, ROMANIA

Minimally invasive approach of a uterine angioleiomyoma in a young patient – case report 10
Ioana Cristina Artene, Iuliana Elena Bujor, Ingrid Andrada Tănase, Iulia Giorgiana Ostafe, Daniela Roxana Mătăsariu, Alexandra Ursache, Irina Dumitrașcu

Congenital methemoglobinemia and uterine leiomyoma – challenges and management 10
Ioana Cristina Artene, Iuliana Elena Bujor, Iulia Giorgiana Ostafe, Alexandra Ursache, Daniela Roxana Mătăsariu, Irina Dumitrașcu

Study of the association of hysteroraphy dehiscence after caesarean section with secondary anemia, subaponevrotic hematoma or wound dehiscence in the postoperative period 11
Ana-Maria Brezeanu, Vlad Iustin Tica

Fetal intraabdominal cysts – report of two cases 11
Iuliana-Elena Bujor, Alexandra Ursache, Daniela-Roxana Mătăsariu, Iulia-Giorgiana Ostafe, Irina Dumitrașcu, Ioana-Cristina Artene

Management difficulties of peritoneal and genital tuberculosis – case report 12
Iuliana-Elena Bujor, Alexandra Ursache, Roxana Chirilă, Daniela-Roxana Mătăsariu, Iulia-Giorgiana Ostafe, Ioana-Cristina Artene, Irina Dumitrașcu

Recurrent acute pancreatitis in a pregnant patient with celiac disease – case report 12
Iuliana-Elena Bujor, Alexandra Ursache, Ingrid-Andrada Vasilache, Daniela-Roxana Mătăsariu, Iulia-Giorgiana Ostafe, Ioana-Cristina Artene, Irina Dumitrașcu

The isthmocele – minimally invasive treatments. Case presentation 13
Iulia Buzdugă, Astia Axenti, Elvira Brătîlă, Andreea Enache

Interstitial ectopic pregnancy – difficult diagnosis and management 13
Alina Călin, Cătălin Herghelegiu

Assessment of the role of hematological inflammatory markers in intrahepatic cholestasis of pregnancy 14
Maria Cemortan

Edinburgh scale – the efficiency of a screening method for the detection of postpartum depression in the SARS-CoV-2 infection context 15
Mădălina Ciuhodaru, Luciana Manole, Diana Popovici, R. Socolov

Ultrasound assessment of first-trimester cystic hygroma and association with karyotype anomalies 16
Diana-Elena Comandașu, Ciprian Andrei Coroleucă, Cătălin Bogdan Coroleucă, Andrei Manu, Elvira Brătîlă

Laparotomy, laparoscopy or robotic surgery? The optimal choice of the approach depending on the complexity degree of the case	17
Bogdan Cătălin Coroleucă, Andrei Manu, Alexandra Băușic, Ciprian Andrei Coroleucă, Diana-Elena Comandașu, Elvira Brătilă	
Brixia score in pregnant critical COVID-19 patients throughout 2021	17
Roxana Covali, Demetra Socolov, Ioana Păvăleanu, Mona Akad, Răzvan Socolov	
Early-onset preeclampsia versus late-onset preeclampsia key points to early action	18
Oana Eliza Crețu, Alina-Alexandra Dîrlău, Cristian Poalelungi, Iuliana Ceaușu	
Anemia in pregnancy – physiology versus pathology	19
Alina-Alexandra Dîrlău, Oana-Eliza Crețu, Adrian Valeriu Neacșu, Djamilă Djafer, Cristian Poalelungi, Iuliana Ceaușu	
The influence of SARS-CoV-2 infection on the maternal mortality rate in the Republic of Moldova	20
Iurie Dondiu, Victor Finciuc, Ana Bîcos	
Oral changes associated with menopause	20
Irina Grădinaru, Cristina Claudia Tărniceriu, Loredana Liliana Hurjui	
Possible oral changes associated with pregnancy	21
Irina Grădinaru, Cristina Claudia Tărniceriu, Loredana Liliana Hurjui	
From asymptomatic bacteriuria to septic shock during pregnancy	21
Corina Grigoriu	
Distribution and pathogens associated with female lower genital tract infection in pregnant and nonpregnant women from Iași city area	22
Loredana Liliana Hurjui, Camelia Grecu, Claudia Cristina Tărniceriu, Diana Popovici, Irina Grădinaru	
Thrombophilia screening – is it useful or not in pregnancy?	22
Loredana Liliana Hurjui, Claudia Cristina Tărniceriu, Diana Popovici, Irina Grădinaru	
Clinical case: management of HIV infection during pregnancy	23
Corina Iliadi-Tulbure, Cristina Bubulici, Maria Cemortan, Cristina Tamazlicar	
16P11.2 deletion syndrome – case report	23
Aurora Ilian, Cristina Secoșan, Simona Brașoveani, Laurențiu Pirtea	
Transplacental transmission of hepatitis C virus infection	24
Dominic-Gabriel Iliescu, Elena-Iuliana-Anamaria Berbecaru, Anca-Maria Istrate-Ofițeru, Rodica Daniela Nagy, Cătălina Rănescu, Alina-Iuliana Enache, Andreea Vochin, Ștefan-Gabriel Ciobanu, Ionuț-Daniel Băluță, Laurențiu Mihai Dîră, Ileana Drocaș, George-Lucian Zorilă	
Lymphadenectomy in gynecological malignancies	24
Alexandra Nicoleta Ioanid, Nicolae Ioanid, Adina Tănase, Sorana Caterina Anton, Nicolae Șerban Ioanid, Mihaela Grigore	
HPV infection – a potential cause for fetal-maternal morbidity?	25
Crîngu Ionescu, Ina Banacu, George Roșu	
The risk of placental thrombosis associated to the infection with SARS-CoV-2	25
Cristina Elena Mandici, Mihaela Grigore, Liliana Claudia Strat, Roxana-Daniela Mătăsariu	
New treatment options in urogenital atrophy	26
Cristina Elena Mandici, Mihaela Grigore, Roxana-Daniela Mătăsariu, Liliana Claudia Strat	
Minimally invasive surgery for apical prolapse	26
Andrei Manu, Bogdan Cătălin Coroleucă, Alexandra Băușic, Ciprian Andrei Coroleucă, Diana-Elena Comandașu, Elvira Brătilă	

The value of weight gain during pregnancy on the evolution of delivery	27
Andriana Marian	
The impact of glypressin in laparoscopic myomectomy	27
Daniela-Roxana Mătășariu, Alexandra Ursache, Cristina-Elena Mandici, Iulia-Giorgiana Ostafe, Iuliana-Elena Bujor, Irina Dumitrașcu	
Research on myoma in Northeastern Romania and socio-medical outcomes	28
Daniela-Roxana Mătășariu, Cristina-Elena Mandici, Iulia-Giorgiana Ostafe, Iuliana-Elena Bujor, Alexandra Ursache	
Genital infection with Ureaplasma urealyticum and pregnancy impact	28
Daniela-Roxana Mătășariu, Alexandra Ursache, Cristina-Elena Mandici, Iulia-Giorgiana Ostafe, Iuliana-Elena Bujor	
PRP (platelet-rich plasma) in infertility	29
Daniela Medinschi, Veaceslav Moșin, Valentina Diug	
The influence of SARS-CoV-2 infection during pregnancy	29
Tiberiu-Ioan Mihalache, Alina Mihaela Călin, Iulian-Valentin Munteanu	
Bowel endometriosis – Bucharest endometriosis center experience	30
Gabriel Mitroi, Anda Simbotin, Francesca Frîncu, Traian Irimia	
Maternal death related to COVID-19	30
Dimitrie Nanu, Călin Popovici, Alma Ștefănescu, Michaela Nanu	
Ovarian pregnancy – case presentation	31
Flavius Olaru, Minodora Ghiga, Ana-Maria Codreanu, Roxana-Oana Micșa, Viorica Iuga, Denisa Giubelan	
Laparoscopy, in vitro fertilization and endometriosis	32
M. Onofriescu, A. Tănase, B. Toma, D. Popescu, D. Țugui	
The uterine microbiome in reproductive medicine	32
M. Onofriescu, A. Tănase, B. Toma, D. Popescu, D. Țugui	
COVID-19 severe pneumonia in a pregnant patient with quadruplets – case report	32
Ioana Păvăleanu, Mona Akad, Maricica Păvăleanu, Răzvan Socolov	
Laparoscopy as a triage test for resectability in advanced ovarian cancers	33
Gheorghe Peltecu, Anca Maria Panaitescu, Nicolae Gică	
Placenta – the key witness of COVID-19 in pregnancy?	33
Liana Pleș, Ioana-Tina Bobei, Gabriel-Petre Gorecki, Gabriel Octavian Olaru, Romina-Marina Sima	
The neonatal consequences of intrauterine infection – herpes simplex virus and Epstein-Barr virus in pregnancy	34
Cezar Podașcă, Sabina Bădilă, Costin Anastasiu, Oana Dimienescu, Cristian Arvătescu, Nicușor Bigiu, Marius Moga	
Probiotic interventions to reduce group B Streptococcus colonization in pregnancy – literature review	34
Cezar Podașcă, Oana Dimienescu, Sabina Bădilă, Andrei Ciubeica, Nicușor Bigiu, Alina Călin, Marius Moga	
Parvovirus B19 infection – harmless virus or pregnancy threat?	35
Dan Popescu, Adina Tănase, Bogdan Toma, Denisa-Oana Zelinschi, Alexandra Ursache, Mircea Onofriescu	
Isthmocele: curing a major surgery complication with minimal invasive techniques	35
Dan Popescu, Adina Tănase, Bogdan Toma, Denisa-Oana Zelinschi, Alexandra Ursache, Mircea Onofriescu	
Prolabation of a pedunculated endocavitary nodule as a result of hemostatic uterine curettage	36
Diana Popovici, R. Socolov, Mădălina Ciuhodaru, Loredana Hurjui, Svetlana Bereșteanu	

Frequency of urinary tract infection in pregnancy	36
Diana Popovici, Mădălina Ciuhodaru, Cătălina Stan, Loredana Hurjui, Svetlana Bereşteanu	
Incidence of vaginal candidiasis in pregnancy	37
Diana Popovici, Răzvan Socolov, Mădălina Ciuhodaru, Cătălina Stan, Loredana Hurjui, Mona Akad, Svetlana Bereşteanu	
Maternal and neonatal outcomes associated with delivery techniques for impacted fetal head at caesarean section – systematic review and meta-analysis	38
Maria Patricia Rada, Răzvan Ciorte, Andrei Măluţan, Ioana Prundeanu, K. Stergios Doumouchtsis, Carmen Bucuri, Ligia Blaga, Dan Mihi	
Maternal anxiety scores correlated with childbirth perineal trauma – preliminary data of a cohort study	38
Maria Patricia Rada, Iulia Ciubotariu, Daniela Matei, Răzvan Ciorte, Andrei Măluţan, Adelina Clim, Viorela Suci, Carmen Bucuri, Doru Diclescu, Dan Mihi	
Urinary infections during pregnancy	39
Viorel Dragoş Radu, Radu Cristian Costache, Veaceslav Groza, Pavel Onofrei, Ingrid Vasilache Tănasă, Valentin Nechifor, Demetra Socolov	
Fetal neurological distress associated to maternal immune activation. Short- and long-term outcome	40
Manuela Cristina Russu	
Voluminous placental chorioangioma complicated with premature placental abruption	41
Cristina Secoşan, Oana Balint, Aurora Ilian, Dorin Grigoraş, Laurenţiu Pirtea	
Surgical challenges during pandemic period	41
Romina-Marina Sima, Anca-Daniela Stănescu, Gabriel-Petre Gorecki, Diana-Cristina Pomană, Liana Pleş	
Group B <i>Streptococcus</i> and pregnancy	41
Anca Angela Simionescu	
Vaccination during pregnancy	42
Anca Angela Simionescu	
Medullary aplasia in pregnancy – obstetrical and maternal risk. Case presentation and literature review	42
Răzvan Vladimir Socolov, Maria Conache-Rusu, Ana-Maria Haliciu, Cristina Tărniceriu	
Maternal group B streptococcal infection/colonization and neonatal consequences	43
Maria Stamatina, Andreea Avasiloaiei	
Increasing patients' confidence in medical-pharmaceutical services	43
Cătălina Daniela Stan, Diana Popovici, Ana Caterina Cristofor, Matei Palimariciu, Magdalena Bîrsan	
Treatment of nosocomial infections with <i>Candida</i> species: clotrimazole versus miconazole	44
Cătălina Daniela Stan, Diana Popovici, Petruţa Smeria, Ana Caterina Cristofor, Matei Palimariciu, Cristina Gabriela Tuchiluş, Magdalena Bîrsan	
Reproduction immunology	44
Nicolae Suci, Ioana Dorobanţu, Mădălina Piron-Dumitraşcu, Ioan-Dumitru Suci	
Female and male infertility in the time of pandemic	45
Adina-Elena Tănase, Bogdan Florin Toma, Dan Popescu, Mircea Onofriescu	
Contraceptive methods in HIV pathology	45
Adina-Elena Tănase, Bogdan Florin Toma, Dan Popescu, Mircea Onofriescu	
Impact of caplacizumab therapy on thrombotic thrombocytopenic purpura in pregnancy: case report and literature review	46
Claudia Cristina Tărniceriu, Irina Grădinaru, Ion Hurjui, Loredana Liliana Hurjui	

Hemophilia in women – from theory to clinical reality	46
Claudia Cristina Tărniceriu, Irina Grădinaru, Ion Hurjui, Loredana Liliana Hurjui	
Pregnancy prognosis after conization for cervical carcinoma <i>in situ</i> – cases and overview of data from literature	47
Mihaela Camelia Țirnovanu, Bogdan Scurtu, Adina Tănase, Roxana Corduneanu, Andreea Crudu, Vlad Gabriel Țirnovanu	
Fetal cardiac evaluation in HIV-positive pregnant women under HAART	47
Alexandra Ursache, Dragoș Nemescu, Iuliana Bujor, Alexandru Luca, Roxana Chirilă, Daniela-Roxana Mătășariu, Dan Popescu, Mircea Onofriescu	
Unusual types of leiomyoma – rare complication of minimally invasive surgery with morcellation	48
Alexandra Ursache, Carmina-Mihaiela Schaas, B. Schaas, Sabina Schaas, Iuliana Bujor, Roxana Chirilă, Monica Țițianu, Daniela-Roxana Mătășariu	
First-trimester screening for aneuploidy in HIV-positive pregnant women under HAART	48
Alexandra Ursache, Dragoș Nemescu, Iuliana Bujor, Roxana Chirilă, Daniela-Roxana Mătășariu, Alexandru Luca, Dan Popescu, Mircea Onofriescu	
The accuracy of placental protein 13 (PP-13) for the first-trimester screening of preeclampsia	49
Ingrid-Andrada Vasilache, Alexandru Cărăuleanu, Demetra Socolov, Roxana Mătășariu, Ioana Păvăleanu, Dragoș Nemescu	
Group B Streptococcus infection in pregnancy	49
Denisa-Oana Zelinschi, Dan Popescu, Adina Tănase, Bogdan Toma, Alexandra Ursache, Mircea Onofriescu	
ZIKV infection in pregnancy	50
Denisa-Oana Zelinschi, Dan Popescu, Adina Tănase, Bogdan Toma, Alexandra Ursache, Mircea Onofriescu	

SUMMARIES OF THE 4TH NATIONAL CONGRESS
OF THE EAST-EUROPEAN SOCIETY OF ENDOMETRIOSIS AND INFERTILITY,
2-4 Iunie 2022, EFORIE NORD, ROMANIA

The preimplantation genetic testing for monogenetic disease (PGT-M) in von Hippel-Lindau syndrome associated with non-obstructive azoospermia	52
Dragoş Albu, Alice Albu	
Ovarian carcinoma associated endometriosis – case reports	52
Ruxandra Albu, Oana Teodor, Florina Păuleţ, Delia Grădinaru, Cristian Peteu, Liviu Popovici, Andreea Marinescu, Adrian Dumitru, Maria Sajin, Monica Cîrstoiu	
Management of premature ovarian insufficiency in patients with endometriosis	53
Mihaela Braga, Elena Griţco, Elvira Brătilă, Andreea Velişcu	
Improving IVF outcome by using DHEA in a patient with two previous failed IVF attempts	53
Viorica Chiriţă, Irina Matei, Carmen Ianiotescu, Ioana Nistor-Mandache, Silviu Predoi	
Endometriosis and endometriosis-related ovarian cancer	53
M.C. Dumitraşcu, C.G. Nenciu, Adina-Elena Nenciu	
New biomarkers in endometriosis – a revision of data from literature	54
Mihaela Grigore, Roxana-Daniela Mătăsariu, Liliana-Claudia Strat, Cristina Elena Mandici	
How to take off the mask of endometriosis... ..	54
Corina Grigoriu	
Septate uterus: diagnosis and treatment	55
Elena Griţco, Mihaela Braga, Tudor Raica, Elvira Brătilă, Andreea Velişcu	
Management of infertility in a patient with stage III endometriosis and poor ovarian reserve	55
Carmen Ianiotescu, Irina Matei, Viorica Chiriţă, Ioana Nistor-Mandache, Silviu Predoi	
Computational models for diagnosing and treating endometriosis	56
Dimitrios Kanellopoulos, Dimitra Karagianni, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
Endometriosis – current management and future trends	57
Dimitrios Kanellopoulos, Dimitra Karagianni, Vasilios Pergialiotis, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
New trends for the medical treatment of endometriosis	58
Dimitrios Kanellopoulos, Dimitra Karagianni, Vasilios Pergialiotis, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
The effect of endometriosis on the quality of life of women	58
Dimitrios Kanellopoulos, Dimitra Karagianni, Vasilios Pergialiotis, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
New approaches to the use of animal models in the study of endometriosis	59
Dimitrios Kanellopoulos, Dimitra Karagianni, Vasilios Pergialiotis, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
Uncovering the genetic basis of female infertility and endometriosis	59
Dimitrios Kanellopoulos, Dimitra Karagianni, Nikolaos Nikiteas, Andreas C. Lazaris, Dimitrios Iliopoulos	
Beyond the uterus and ovaries. Transvaginal ultrasound as the first line of diagnosis in deep infiltrative endometriosis	60
Radu Maftai	

KIR-HLAC genotyping can assess the human reproductive success	60
Irina Matei, Carmen Ianiotescu, Viorica Chiriță, Ioana Nistor-Mandache, Silviu Predoi	
Fertility management in patients with severe endometriosis	60
C.G. Nenciu, M.C. Dumitrașcu, Adina-Elena Nenciu	
First laparoscopy or IVF in endometriosis with infertility	61
M. Onofriescu, Adina Tănase, B. Toma, D. Popescu, Denisa Țugui	
A rare case of thoracic endometriosis syndrome	61
Nuți Daniela Oprescu, Bianca Mihaela Danciu, Elena Theodora Giubegeanu, Mona Khraibani, Gabriela Adriana Dinca	
Clear cell carcinoma in ovarian endometriosis: a not so rare malignancy arising at a very uncommon age – case report and literature review	62
Nuți Daniela Oprescu, Elena Theodora Giubegeanu, Simona Alina Dascălu, Bogdan Staicu, Bianca Mihaela Danciu, Tiberiu Augustin Georgescu	
Is there success in pursuing novel treatment options for women with endometriosis?	62
Aida Petca, Ioana Gabriela Calo, Andreea Borislavschi, Răzvan-Cosmin Petca, Mihaela Boț	
Parietal endometriosis: a challenging disease	63
Maria Sidonia Săndulescu, Lorena Dijmărescu, Sidonia Cătălina Vrabie, Ioana Camen, Cristina Ștefănescu, Mariana Dumitrica, Cosmina Grigorie, Maria Magdalena Manolea	
The endometriosis patients’ quality of life – how can it be evaluated and improved?	63
Romina-Marina Sima, Anca-Daniela Stănescu, Octavian-Gabriel Olaru, Liana Pleș	

SUMMARIES OF THE 7TH NATIONAL CONFERENCE
OF THE ROMANIAN SOCIETY OF HPV,
2-4 Iunie 2022, EFORIE NORD, ROMANIA

Practice points in cervical precancer detection	64
Mihaela Badea, Irina Julea, Elena Popa, Corina Grigoriu, Miruna-Ruxandra Burcin	
New evidence on efficacy of one-dose human papillomavirus (HPV) vaccine against cervical cancer	64
Mihaela Boț, Bianca Miron, Aida Petca, Radu Vlădăreanu	
The HPV vaccine – between social media myth and reality	65
Anca Burnei, Vlad Zamfirescu, Andrei Trăistaru, Andra Maria Lorentz, Dragoș Tudorache, Radu Vlădăreanu	
The value of cytotumor examination in the diagnosis of dysplasia and cervical cancer. The new approach to cervical screening	65
Gheorghe Cruciat, Andreea Florian, Iulia Popa, Mariam Chaikh	
Colposcopic findings among women with high-risk HPV	66
Gabriela Adriana Dinca, Bianca Mihaela Danciu, Elena Eni, Tudor Galbur, Cristiana Victoria Dragotoiu, Nuți Daniela Oprescu	
Clinical and virological risk factors involved in premalignant and malignant lesions of the uterine cervix – particular features in Romanian patients	66
Marina Dudea-Simon, Ioana Berindan-Neagoe, Laura Ancuța Pop, R. Ciortea, A. Măluțan, D. Diculescu, S. Vesa, Mihaela Oancea, Renata Nicula, R. Mocan-Hognogi, C. Porumb, D. Mihu	
Residual disease and/or CIN 2-3 recurrence – the practical approach	67
Corina Grigoriu	
Adjuvant HPV vaccination in the prevention of recurrent HSIL lesions after electrosurgical treatment	67
Laura Leonte	
The role of microbiome in persistent HPV infection	68
Mihai Mitran, Sorin Puia, Roberta Deaconescu, Maria Olinca, Elvira Brătilă	
Societal costs and economic burden of the frail HPV vaccination policy – a Romanian reality	68
Aida Petca, Ioana Gabriela Calo, Andreea Borislavski, Răzvan-Cosmin Petca, Mihaela Boț	
Antiviral interventions for HPV: current challenges and options	69
Ana-Cătălina Savu, Anca Popa, Manuela Cristina Russu, Șerban Nastasia	
Vaccination after surgical treatment for CIN	69
Ana-Cătălina Savu, Anca Popa, Manuela Cristina Russu, Șerban Nastasia	
Genital HPV keratotic lesions – differential diagnosis based on dermoscopic findings	70
Florica Șandru, Adelina Popa, C.G. Nenciu, M.C. Dumitrașcu	
Urinary HPV DNA testing – the method of increasing cervical screening	70
Octavia Velicu, Elvira Brătilă, Mihai Mitran	

Minimally invasive approach of a uterine angioleiomyoma in a young patient – case report

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Introduction. Angioleiomyoma is a benign tumor, characterized by a mixture of smooth muscle cells and dilated thick-walled blood vessels. The uterine location of the angioleiomyoma was rarely reported, being more common in middle-aged women. Preoperative diagnosis is very difficult due to the leiomyoma-like aspect on ultrasound examination and the nonspecific clinical manifestations such as abdominal mass, abdominal pain or menorrhagia. The histological examination and the immunohistochemical staining are necessary for the final diagnosis. **Case report.** We report a case of uterine angioleiomyoma diagnosed in a 23-years old woman, treated by laparoscopic excision of the nodule, followed by uterine angioembolization. The patient presented with moderate anemia due to a nine-month history of worsening menorrhagia and intermittent left iliac pain. Transvaginal ultrasound examination showed an enlarged uterus with heterogeneous and hypoechoic lesions of 1.5 cm in the posterior myometrium, respectively a 3-cm nodule located in the anterior myometrium with

protrusion in the uterine cavity, both with increased vascularity. A laparoscopy intervention was performed and two uterine nodules were identified. During the excision of the uterine nodules, the exteriorization of a cerebroid consistency soft tissue with cystic areas of dark brown blood was observed. The diagnosis of uterine angioleiomyoma was final after histological examination and immunohistochemical staining. An angioembolization procedure was performed one year later and the intracavitary angioleiomyoma was eliminated. **Conclusions.** Uterine angioleiomyoma is an extremely rare condition that usually occurs in middle-aged females. The recommended treatment is angiomyomectomy or hysterectomy depending on the patient’s symptoms and her desire to preserve fertility. For a young female, a minimally invasive approach should be considered. An embolization procedure may be a successful treatment alternative for submucosal angioleiomyoma.

Keywords: angioleiomyoma, abdominal mass, abdominal pain, menorrhagia

Congenital methemoglobinemia and uterine leiomyoma – challenges and management

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Introduction. Methemoglobinemia is characterized by the presence of an abnormally increased level of an oxidized form of hemoglobin. This form of hemoglobin does not carry oxygen properly to the tissues. In contrast with the pharmacologically induced form, congenital methemoglobinemia is rarely diagnosed, and it is caused by innate cytochrome B5 deficiency or cytochrome b5 reductase deficiency. Although not lethal, this condition can aggravate other diseases of the patient due to tissue hypoxia. **Case presentation.** We present the case of a 43-years-old woman diagnosed with congenital methemoglobinemia that presented important metrorrhagia and hypogastric pain. The clinical examination revealed cyanotic discoloration of the skin without respiratory distress and the presence of an enlarged and irregular uterus. The transvaginal ultrasound examination described a uterus with multiples leiomyomas with a maximum diameter of 7 cm. After six months of treatment with iron and vitamin C supplements, a classical total hysterectomy was

performed. The surgery went without intraoperative complications, the patient was stable, but her baseline oxygen saturations measured by a conventional pulse oximeter was around 60%. The patient did not receive any specific treatment for congenital methemoglobinemia, like blue methylene, due to her stable condition and she was discharged three days later. **Conclusions.** The treatment for congenital hemoglobinemia is necessary for conditions like sepsis, cerebrovascular disease, pulmonary disease, coronary disease, acidosis or anemia, because tissue hypoxia may occur even in patients with a low level of methemoglobin. The oxygen saturation should be measured by co-oximetry, because the standard pulse oximeter may indicate an alarmingly low oxygen saturation. Knowing the baseline of oxygen saturation of the patient, the use of co-oximetry, determinations of “saturation gap” and a complete evaluation of the patient’s conditions are the best approach for these types of cases.

Keywords: methemoglobinemia, uterine leiomyoma

Study of the association of hysteroraphy dehiscence after caesarean section with secondary anemia, subaponevrotic hematoma or wound dehiscence in the postoperative period

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Introduction. The incidence of caesarean section has increased significantly in recent years. This is a retrospective and observational study, over a period of five years (from April 2017 to April 2022). The present paper aims to show the correlation between the dehiscence of the hysteroraphic tranche with anemia, the postoperative hematoma or the dehiscence of the skin wound in the postoperative period. **Working method.** This study was performed on a group of 5562 patients who gave birth by caesarean section, and found four patients who met the inclusion criteria. The inclusion criteria were secondary anemia, subaponevrotic hematoma or cutaneous wound dehiscence, associated with uterine dehiscence, resulting in hysterectomy of necessity.

Results. All patients with uterine dehiscence resulting in hysterectomy necessitated secondary anemia and subaponevrotic hematoma, one case of which was associated with supraaponevrotic hematoma, but none of them were associated with cutaneous wound dehiscence.

Conclusions. Out of the studied group of 5562 patients, 16 patients developed subaponevrotic hematomas, four of them developing uterine hysteroraphy dehiscence and requiring a hysterectomy of necessity, with an incidence of 25%. In the literature, the hysterectomy of necessity after the appearance of a subaponevrotic hematoma is between 25% and 98%.

Keywords: hysteroraphy, dehiscence, hematoma, secondary anemia, postoperative wound

Fetal intraabdominal cysts – report of two cases

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Introduction. With the widespread use of routine ultrasound during pregnancy, the incidence of fetal intraabdominal cyst finding is relatively common and is most frequently detected in the second or third trimester. Despite the fact that many of these formations disappear spontaneously without long-term clinical consequences, a correct prenatal diagnosis is essential both for the optimal counseling of the parents and to establish a proper prenatal and postnatal management. **Case description.** In this paper, we report two cases of antenatally-detected fetal intraabdominal cysts, in male and in female fetuses. *Case 1.* A 31-year-old woman, at her first pregnancy, was referred to our center at 32 weeks of gestation for routine ultrasound during which a transonic tumor of approximately 5/4 cm was discovered. The pregnancy was ultrasound monitored every two weeks and the cyst reached the size of 10/8.5 cm at 37 weeks. She delivered at 38 weeks a female infant, weighing 3220 g. The newborn

was operated on the first day of life and the anatomical-pathological result described a simple serous ovarian cyst. *Case 2.* A 30-year-old woman was referred to our center at 17 weeks for routine scanning. Ultrasound examination revealed 7 mm and 5 mm bilateral choroid plexus cysts, micropenis and an intraabdominal, unilocular and anechogenic 18-mm cyst. The patient was evaluated every two weeks and the cyst disappeared until the patient reached the term. **Conclusions.** There are different types of fetal intraabdominal cysts that differ by their origin, the site of occurrence and have a diverse impact on fetal development. There are differences between the etiology of intraabdominal cysts in male and female fetuses, resulting in differences in prenatal and postnatal care. Despite the high risk of surgery at birth, the long-term outcome is good in the majority of cases.

Keywords: fetal intraabdominal cyst, pregnancy, ultrasound

Management difficulties of peritoneal and genital tuberculosis – case report

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Introduction. Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, which mainly involves the lungs. Primary genital infections are extremely rare and may occur if the partner has active genitourinary TB. In women, genital tuberculosis symptoms mimic other gynecological conditions which makes the diagnosis difficult due to the lack of distinct features. **Case description.** We report the case of a nulliparous 45-year-old woman which accuses bilateral iliac fossa pain and genital bleeding for about six months. The initial evaluation included transvaginal ultrasound examination, pelvic MRI and the measuring of CA-125 serum level. The imagistic evaluation reveals a left ovary with a tumoral mass with suspicious features and an enlarged uterus due to multiple fibroids, each one of them being under 30 mm. Considering the normal levels of CA-125, two possibilities of diagnosis seemed to be more plausible: dermoid cyst or tubal pathology. To establish the final diagnosis, we decided to perform laparoscopic surgery. The severity of the adhesion syndrome forced

us to convert the intervention to classic laparotomy. We hardly performed a total hysterectomy with bilateral salpingo-oophorectomy. During the intervention, we noticed a 2-cm sigmoid colon injury that required a colostomy. The anatomic pathology report established the diagnosis of left tubo-ovarian and peritoneal tuberculosis. Following the diagnosis, the patient began the treatment with standard antituberculosis drugs. **Conclusions.** The reported case had no history of pulmonary tuberculosis, the chest X-rays performed before surgery was normal and, also, the patient did not present any indirect evidence that suggested the diagnosis of genital and peritoneal tuberculosis, such as ascites or elevated CA-125 levels. Genital tuberculosis is a rare form of TB. The diagnosis and the treatment remain challenging, particularly because there are no specific laboratory test and imaging evaluations to differentiate this disease from others.

Keywords: *Mycobacterium tuberculosis*, genital tuberculosis

Recurrent acute pancreatitis in a pregnant patient with celiac disease – case report

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Introduction. Despite the low incidence during pregnancy, acute pancreatitis (AP) is associated with a high rate of maternal-fetal mortality. The most common factors that cause AP are gallstones, abuse of alcohol and hyperlipidemia, but idiopathic pancreatitis is also reported. Depending on the severity of the disease and the time of onset, the treatment varies from a conservative approach to endoscopic retrograde cholangiopancreatography. **Case presentation.** We present the case of a 25-year-old patient with 34 weeks of amenorrhea who presented severe epigastric pain, nausea and vomiting. She was diagnosed with celiac disease and she had three episodes of AP over the last three years. The diagnosis of idiopathic AP was based on clinical presentation, laboratory tests that showed leukocytosis, raised amylase and lipase serum levels, and based on the ultrasound examination: bulky pancreas with peripancreatic

fluid. She was managed conservatively, and after six days she prematurely gave birth to a healthy newborn, G=1900 g, Apgar score 8-9. On the fifth day after birth, a computed tomography scan of the abdomen was performed and the results showed a bulky pancreas, the presence of fluid in the left parietocolic space, infiltration of peripancreatic fat and intestinal edema. During the postpartum period, the patient’s condition and her blood tests improved, and she was discharged two weeks later. **Discussion.** Acute pancreatitis in pregnancy is a rare but severe event, and it most commonly occurs in the third trimester. The diagnosis, etiology and severity of pancreatitis are established based on clinical, biochemical and ultrasound examinations. If possible, the treatment should be conservative, at least until the delivery of the baby.

Keywords: pancreatitis, pregnancy, celiac disease

The isthmocele – minimally invasive treatments. Case presentation

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Introduction/objective. The isthmocele represents a discontinuity of the anterior uterine wall that appears as a result of a deficient healing at the level of hysterorraphy after caesarean section, which involved both gynecological and obstetric complications. Depending on the thickness of the overlying myometrium, there may be a large defect, affecting more than 50% of it, or a small defect with an interest of less than 50% or a thickness of more than 3 mm of the myometrium. This classification is important in the therapeutic decision to establish a hysteroscopic or laparoscopic treatment. **Methodology.** The present paper aims to present the case of a 27-year-old patient who presents to the clinic for secondary infertility,

dysmenorrhea, intermenstrual spotting and severe dyspareunia. Ultrasound examination reveals a wide niche after caesarean section. **Results.** The patient undergoes laparoscopic correction of the isthmocele. The follow-up at six weeks postoperatively showed a significant improvement of symptoms and a normal ultrasound examination, with the disappearance of the niche. **Discussion and conclusions.** Although a still incompletely understood entity, the diagnosis of isthmocele is constantly increasing, which is why the treatment should be chosen depending on the presence of symptoms, the size of the defect, the secondary infertility and the desire to conceive.

Keywords: isthmocele, minimally invasive treatments

Interstitial ectopic pregnancy – difficult diagnosis and management

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Introduction. An interstitial pregnancy occurs when the ectopic gestation is implanting in the interstitial part of the fallopian tube. Interstitial pregnancy accounts for 2-6.8% of all ectopic pregnancies. The increase in the incidence of interstitial pregnancy is mostly due to improvements in ultrasound diagnosis and uptake of assisted reproductive techniques. **Materials and method.** Interstitial pregnancy is a subtype of tubal ectopic pregnancy. It could be classified as partial or complete. Diagnosing interstitial pregnancy may be difficult due to the similar presenting symptoms and signs with other ectopic pregnancies and to difficulties in distinguishing an interstitial preg-

nancy from an eccentric intrauterine or isthmic tubal ectopic pregnancy on ultrasound imaging. Transvaginal ultrasound scan is the primary diagnostic, and 3D ultrasound and MRI may be helpful for delineating the gestational sac's location in difficult cases. **Results.** There is a high risk of maternal mortality due to the challenge of timely diagnosis and a high risk of rupture of the interstitial pregnancy, causing catastrophic consequences. **Conclusions.** The surgical management, with a higher rate of success, must be done in centers with a good surgical experience.

Keywords: interstitial pregnancy, ultrasound, management

Assessment of the role of hematological inflammatory markers in intrahepatic cholestasis of pregnancy

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Background. Intrahepatic pregnancy cholestasis (ICP) is a condition characterized by an increase in serum bile acid (BA) and liver function tests in the presence of skin pruritis. Given that high BA values cause the release of proinflammatory mediators, the authors propose that hematological inflammatory markers in the ICP, such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), mean platelet volume (MPV), erythrocyte distribution index, standard deviation of the erythrocyte distribution index (RDW-SV) and coefficient of variation of the index (RDW-CV), undergo some changes. **Materials and method.** The prospective study was carried out by assessing 120 cases, divided into two groups: Group A – 60 women, whose pregnancy was complicated by ICP; and Group B – 60 cases without ICP. The χ^2 test without Yates’ correction for continuity was applied to compare the categorical variables. **Results.** The assessment of the BA level revealed the following mean values: $37 \pm 5.1 \mu\text{mol/l}$ in Group A (ranging between

10 and $211 \mu\text{mol/l}$) and $3.47 \pm 0.2 \mu\text{mol/l}$ in Group B. Protein C-reactive was assessed in both groups, and elevated values were detected in seven cases in Group A and in 10 cases in Group B ($\chi^2=0.617$, $p=0.4322$). The mean values of hematological inflammatory markers were: NLR – 5 ± 0.4 in Group A, compared with 4.7 ± 0.3 in group B; PLR – 151.5 ± 7.8 in Group A and 124.8 ± 5.8 in Group B; MPV – 11.5 ± 0.1 fl in Group A and 11.4 ± 0.1 fl in Group B; RDW-SV – $46.5 \pm 0.8\%$ in Group A and $48.6 \pm 0.8\%$ in Group B; RDW-CV – 14.2 ± 0.3 fl in Group A and 14.6 ± 0.2 fl in Group B. **Conclusions.** The study revealed an increase in PLR values in the group of women whose pregnancy was complicated by ICP, compared to the control group. However, further studies with a larger number of participants are required in order to draw conclusions about the role of hematological inflammatory markers in intrahepatic cholestasis during pregnancy.

Keywords: intrahepatic cholestasis of pregnancy, cholestasis gravidarum, pregnancy

Edinburgh scale – the efficiency of a screening method for the detection of postpartum depression in the SARS-CoV-2 infection context

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As postpartum depression is the most common complication in pregnancy (more frequent than gestational hypertension)/with 13% pregnant women affected by psychiatric diseases in context of the lack of peripartum screening where are a lot of risks factors such as hormonal decline after birth and any kind of stressful events, familial history of affective disorders, family problems and lately social isolation due to COVID-19.

Objectives. The use of Edinburgh Scale as a primordial and a reliable screening method in order to help family doctors and obstetricians to evaluate the risk of postpartum depression (PPD) especially in the context of SARS-CoV-2 infection. **Materials and method.** We used as an anonymous enquiry, formed by 10 questions regarding the way the tested woman felt during the last week and making total difference between anxiety, phobias, or personality disorders. The evaluator should be extremely attentive to question number 10 which shows the risk of suicidary thoughts. The enquiry included 14 COVID-19 patients from obstetrics and gynecology hospitals and someone was available on the phone (free of charge) for who asked for psychological counseling/lactation support with SAMAS (Health Program for Mothers and Neonates). The maximum score is 30 and a score bellow 10 represents clearly a risk for depression, while a score above 13 certify the diagnosis of moderate or even severe depression. **Results.** With a satisfying specificity (78%) and a good predictor value (73%), along with quite good sensitivity (86%), the Edinburgh scale represents a reliable instrument to detect PPD. From the 462 women infected with SARS-CoV-2, 42% have been affected by mild depression manifested primordially as reluctance/refuse to lactate, asthenia, disturbed sleep

pattern, multimodal disorders or mood disorders, nutritional disorders, affected libido etc.; 73% of the patients presented with anxiety, 2% had phobias, and 1.2% had different personality disorders. Depression was mildly affecting mostly women living in urban areas (57.3%), compared to rural areas (43.7%). Most frequently, depression had affected woman at extreme ages (16-18 years old and over 40 years old – 49%), probably due to pregnancy-related symptoms. There is a strong demonstrated relationship between the existence of family history or PPD, anxiety, body image disorders etc., with an increase of 17% females affected. The waves of SARS-CoV-2 infections together with the restriction and social isolation determined PPD (41.3%), anxieties (31.3%), phobias (1.2%) and personality disorders (26%). As the psychological counseling was thoroughly provided priorly, there was a vast majority with no psychiatric medical management needed (42.3%) copying lately with heavy maternal duties. **Conclusions.** Social isolation due to SARS-CoV-2 infection is manifested as a large pallet of anxiety or mood changes going to mild depression or phobia which proved the necessity of postpartum counseling. If we added the instruction of family doctors or obstetrics and gynecology by providing a straight protocol for PPD screening using Edinburgh Scale as major instrument for detection, we might make a diagnosis and perform a therapeutic approach of PPD, to repet the evaluation, especially the three factors: depression – questions 1, 2 and 8; anxiety – questions 3, 4 and 5 and suicide (question 10), being quite perfect for a good evaluation.

Keywords: postpartum depression, anxiety, suicide, SARS-CoV-2, Edinburgh Scale

Ultrasound assessment of first-trimester cystic hygroma and association with karyotype anomalies

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Cystic hygroma represents a fluid accumulation in different structures, often cephalic, on the left side, with an incidence of 1/6000-1/16,000. Karyotype anomalies are found in 20-75% of cases, most frequently Turner, Down, Klinefelter, Edwards and Patau syndromes. Subchromosomal abnormalities include Noonan syndrome, Fryns syndrome, multiple pterygium syndrome and achondroplasia, and also maternal alcohol consumption. We report a series of cases diagnosed in the first trimester with cystic hygroma and their genetic determinacy. The first patient was diagnosed at 11.6 weeks of gestation with a large cystic lesion sheltering the entire fetus, with omphalocele, AVSD and arthrogyriposis. The patient decided the termination of pregnancy and the karyotype confirmed the Down syndrome. The second patient, having a term birth by caesarean section followed by five first-trimester miscarriages, presented at 8.5 weeks of gestation, with an ultrasound image of large cystic hygroma causing double contour suggestive for fetal hydrops and no fetal heartbeat. The abortion product karyotype revealed Turner syndrome. Couple karyotyping and genetic counseling were recommended, showing a 46,XX/47,XXX mosaicism in the mother, re-

spectively an addition in the 9th pair of chromosomes in the father – 46,XY,add(9)(p12), for which arrayCGH was recommended in order to detect a possible chromosomal balanced translocation, which was ruled out. The third patient, with history of two early pregnancy miscarriages and two failed IVF procedures, presented with a spontaneous 11.6-week pregnancy showing cystic hygroma, medium size omphalocele, micrognathia and hypoplastic nasal bone. The parents decided the termination of pregnancy and the karyotype revealed trisomy 18. The fourth patient was diagnosed in the first trimester with a large left laterocervical cystic mass, consistent with lymphangioma. The follow-up showed normal development and amniocentesis revealed a normal karyotype. An appropriate weight neonate was born at 38 weeks by caesarean section, with a good postnatal transition, expecting removal surgery of the cervical lymphatic cyst sized 12 cm. We suggest a significant association between cystic hygroma and karyotype anomalies, stronger in patients with obstetrical failure history, validated by invasive genetic testing.

Keywords: cystic hygroma, karyotype anomalies, first-trimester ultrasound

Laparotomy, laparoscopy or robotic surgery? The optimal choice of the approach depending on the complexity degree of the case

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Introduction. The use of minimally invasive surgery with robotic assistance has grown exponentially since its approval. Applications include benign afflictions and staging and management of gynecological malignancies. The rapid adoption of robotic technology comes from the enhanced visualization, wristed instrumentation, and improved ergonomics inherent to such systems, enabling more surgeons to perform minimally invasive procedures previously restricted to surgeons with advanced laparoscopic skills. Such technology may also enable those with laparoscopic experience to perform more complex cases that would otherwise require open techniques. Compared with traditional laparoscopy, robotic platforms are promoted as resulting in less blood loss, less postoperative pain, shorter hospital stay, and higher lymph node retrieval, although perhaps at the expense of cost. Compared to robotic surgery, laparoscopic surgery has certain limitations, such as two-dimensional imaging, restricted range of motion of the instruments, and poor ergonomic positioning of the surgeon. **Materials and method.** In this paper, we present our personal experience of 1171 surgical interventions regarding laparotomy versus laparoscopy versus robotic surgery. **Results.** Although the available literature suggests that robotic and laparoscopic techniques seem to be no different for many outcomes, there is compelling evidence that robotics has advantages over open techniques. Of the three outcomes that we believed had the most critical effect on patient care (operative time, length of hospital stay, and days to return to normal activity), there

was a consistent trend toward reduced length of stay for robotic surgery compared to laparotomy. A total of 1171 interventions have been performed either by laparotomy, vaginal, laparoscopic or robotic. Out of these, 491 (41.92%) were performed laparoscopically and 83 were performed robotically (7.08%). Regarding the indications of the interventions, 414 (84%) laparoscopic interventions were performed for benign afflictions and 77 (16%) for malignancies. From the 83 robotic surgeries, 56 (75.9%) were performed for benign diseases and 20 (24.1%) were performed for malignancies. The cases of complex comorbidities, such as severe adhesions, obesity or deep infiltrating endometriosis, are well suited for robot-assisted surgery. More extensive interventions in deep infiltrating endometriosis with partial resection of the bowel or bladder can also be performed with lower complication rates by this minimally invasive approach. The use of robotic surgery for malignant gynecological diseases is increasing in proportion to centralization and the availability of the robot. The use of the robot may be meaningful even in fertility-conserving operations like trachelectomy. **Conclusions.** Overall, there seems to be an advantage to robotic techniques over traditional open surgery in the management of gynecological afflictions. Therefore, the specific method of minimally invasive surgery, whether laparotomy, conventional laparoscopy or robotic surgery, should be tailored to patient selection, surgeon ability and equipment availability.

Keywords: laparoscopic surgery, robotic surgery, laparotomy, complex cases

Brixia score in pregnant critical COVID-19 patients throughout 2021

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Background. The evolution of pregnant critical COVID-19 patients is unpredictable. **Methodology.** The patients admitted to the COVID-19 intensive care unit of the "Cuza Vodă" Clinical Hospital of Obstetrics and Gynecology in Iași between January 1st and December 1st, 2021, with critical forms of the disease (n=21) were included and retrospectively studied. Brixia scores (H – highest, L – lowest, A – upon admission, and E – when hospitalization ended) were calculated from their chest X-rays. The patients' age range was 25-52

years old. **Results.** Both A score and E scores decreased throughout the year 2021, due to the progress in patient management. The highest scores were close to the admittance scores, while the lowest scores were not always the ones obtained when hospitalization ended. **Conclusions.** Most critically ill pregnant COVID-19 patients improved their respiratory function throughout hospitalization, but the evolution was not as linear as expected.

Keywords: COVID-19, pregnancy, Brixia score

Early-onset preeclampsia versus late-onset preeclampsia key points to early action

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Introduction. Preeclampsia is one of the top five causes of maternal and perinatal morbidity and mortality worldwide and is associated with a higher risk of complications for both mothers and babies. Great advances in preeclampsia screening have been made over the decades. The key to maintaining optimal screening performance is to establish standardized protocols for biomarker measurements and regular biomarker quality assessment. **Methodology.** Preeclampsia is divided into early-onset and late-onset, according to the time of onset. The etiology of early-onset form of preeclampsia is related to incomplete trophoblast invasion and failure of normal spiral artery remodeling. Late-onset preeclampsia is associated with increased maternal vascular susceptibility to the normal inflammatory state of pregnancy or atherosclerosis of a placenta grown initially normal. **Results.** The angiogenic imbalance between PlGF and sFlt-1 has a pivotal role in the pathogenesis of the disease, and their ratio is a useful tool in its prediction. The decrease in the PlGF level is evident as early

as the beginning of the second trimester of pregnancy, before the development of signs and symptoms of the disease. sFlt1/PlGF ratio has the highest accuracy for differentiating preeclampsia patients from normal pregnant women, and it could help in diagnosing high-risk women for developing preeclampsia, decreasing costs related to serious maternal and neonatal complications by precise observation and early medical interventions. **Discussion.** A major challenge in modern obstetrics is the early identification of pregnancies at high risk of early-onset preeclampsia and undertaking the necessary measurement to improve placentation and reduce the prevalence of the disease. The additional value of first-trimester screening combined with the value of the sFlt-1/PlGF ratio as an aid in the diagnosis of preeclampsia and short-term prediction along with the prediction of adverse outcomes provide a complete solution for preeclampsia throughout pregnancy.

Keywords: preeclampsia, screening for preeclampsia, guidelines

Anemia in pregnancy – physiology versus pathology

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Introduction. Although effective interventions are currently available to address anemia and efforts have been made to increase awareness and action, anemia remains a global public health problem that particularly affects young children and pregnant women, with an important impact on pregnancy outcomes and on maternal and infant health. **Methodology.** A small retrospective observational study was conducted in the Obstetrics and Gynecology Department of the "Dr. I. Cantacuzino" Clinical Hospital, respecting current diagnostic criteria recommended by World Health Organization (WHO) and regional guidelines (hemoglobin concentration <11 g/dL before/after birth) on a sample of 200 cases of pregnant women diagnosed with maternal anemia at the moment of delivery, a part of the total of 1824 pregnant women with anemia from 2962 births who were admitted in our hospital between the 1st of April 2019 and the 31st of March 2021, taking into consideration the COVID-19 outbreak and its major impact on healthcare policies. The aim was to assess the screening, the follow-up and the therapeutic problems and bring under discussion the clinical cases and evidence-based information regarding early diagnosis and treatment of pregnancy anemia. **Results.** Pregnancy induces significant demands in a woman's body and triggers many physiologic adaptations which can lead to maternal anemia due to hematological and iron balance changes, in the same way that can reveal and magnify undiagnosed underlying pathologies.

Iron deficiency (ID) is the most common cause of anemia in pregnancy, affecting more than half of pregnancies and the opportunity of iron supplementation during pregnancy and during postpartum period is heavily debated, including when and how to initiate the treatment in order to improve pregnancy outcomes and to lower the complications on women's and infant's health. In our experience, the pandemic group had poor or no follow-up during the pregnancy in comparison with the period before, and needed more intravenous iron therapy or blood products administration, with the necessity of longer hospitalization periods and higher peripartum complications and premature birth rate. Although most prenatal guidelines recommend screening for anemia in pregnancy, recommendations for ID screening are variable, and thus ID screening practices among clinicians are inconsistent. Only a small percentage in our group (10%) were ID screened in the first trimester of pregnancy using ferritin levels, with a lack of data in the second and third trimesters. **Conclusions.** The issue of physiology versus pathology remains questionable, the physiological ranges for pregnancy itself need to be better statuated, and future research needs to focus on developing screening instruments and improve therapeutic strategies in order to reduce anemia among pregnant women and its complications.

Keywords: pregnancy anemia, iron depletion, pregnancy complications

The influence of SARS-CoV-2 infection on the maternal mortality rate in the Republic of Moldova

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Introduction. COVID-19 pandemic remains one of the most difficult challenges facing humanity since the beginning of the 21st century. Since March 2020 until March 2022, a total of 513,442 cases and 11,431 deaths were reported in the Republic of Moldova, which corresponded to a mortality rate of 2.2%. The pandemic has led to social isolation measures, which have limited the population’s access and addressing rate to healthcare services, including pregnant women. **Materials and method.** A retrospective monitoring study of maternal mortality (MM) in the Republic of Moldova during 2020-2021 due to COVID-19 cases in pregnant women was performed. SPSS version 3 was used for data processing. **Results.** In the Republic of Moldova, from a total of 19 deaths (31 per 100,000 live births) among pregnant women, 68% (13 deaths) were associated to COVID-19. The average age of the patients was 29.6 years old. The primiparous/secondiparous ratio was 1:1. In 70% of patients, preexisting pregnancy comorbidities were found (viral hepatitis, chronic bronchitis, hypertension, chronic pyelonephritis). More than 30% of women were overweight. Pregnancy was complicated with iron deficiency anemia in 50% of cases, imminent abortion appeared in 20% of cases, and

for each of the following: gestational diabetes, hydronephrosis and gestational hypertension, the rate was 10%. None of the women were vaccinated against SARS-CoV-2 and did not suffer from the disease before pregnancy. Severe acute respiratory syndrome developed on the seventh day of illness in 40% and after 10 days in other 60% of cases. In postpartum females, death occurred in 80% of the cases. Emergency caesarean section (ECS) was performed in 50% of cases. In all cases, the indication for ECS was the worsening of respiratory failure’s degree. From all pregnant women, 30% gave birth *per vias naturales*. From the onset of the first disease’s symptoms until death occurred, an average, 21.3 days have passed. In all cases, the disease was complicated with sepsis, MODS, pulmonary embolism and cardiorespiratory arrest. **Conclusions.** It can be observed that the MM rate in the Republic of Moldova increased significantly during the COVID-19 pandemic. This can be explained by the high contagiousness of the disease, mainly in 2021 (10 deaths), the low vaccination rate among pregnant women during that period in the Republic of Moldova and the delayed addressing of pregnant women to medical services.

Keywords: COVID-19, maternal mortality, pandemic

Oral changes associated with menopause

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Introduction. During the evolution of a woman’s life, menopause is a normal process, being the result of irreversible hormonal changes and ovarian reproductive function. Menopause is a physiological process that is accompanied by a series of characteristic changes, some of which can be found at the oral cavity level. The purpose of this paper was to detect and evaluate the changes in the tissues of the oral cavity in menopausal women. **Methodology.** PubMed and Scopus databases were searched using the keywords “oral cavity” and “menopause”. **Results.** Data from the literature locate oral changes at various levels of the stomatognathic system: gingival (covering the appearance of gingivitis/periodontitis), mucosal (stomatitis), bone (demineralization with faster loss of alveolar bone), tongue (glosodinia on isolated segments/diffuse), salivary glands (changes in salivary pH, decreased salivary secretion with the appearance of dry mouth), taste receptors (altered taste perception with

the appearance of sour/salty/metallic taste etc.). Vascular type algae (“painful mouth syndrome”), painful syndromes located in the alveolar bone or in the temporo-mandibular joint have also been found during menopause, often influenced by the contraceptive treatment. **Conclusions.** Oral changes associated with menopause are often influenced by previous contraceptive treatments. It is necessary to detect them as early as possible in order to improve the symptoms, prevent the possible complications and institute the treatment in the various compartments of the stomatognathic system during the involution period. The approach and therapy in such situations will be complex, interdisciplinary (dentist-gynecologist- endocrinologist), addressing both the body in general and the elements of the stomatognathic system, in order to install the homeostatic balance.

Keywords: menopause, oral pathology, osteoporosis, stomatitis

Possible oral changes associated with pregnancy

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Introduction. Pregnancy is a physiological process during which dishomeostatic phenomena occur with an impact on the stomatognathic elements. Pregnancy is characterized by profound metabolic and functional changes, hormonal imbalances (the appearance of new hormones and the increase of existing ones normally during the menstrual cycle). This paper aimed to detect and evaluate the possible changes in oral tissues in pregnancy. **Methodology.** PubMed and Scopus databases were searched using the keywords "oral cavity" and "pregnancy". **Results.** The data from the literature draw attention to the possibility of changes in the tissues of the oral cavity during pregnancy. Subjective clinical examination reveals the presence of a variety of symptoms, mainly dental (pain), periodontal (embarrassment, tension and gingival discomfort, itching, tenderness and bleeding when chewing), dry mouth and hyposalivation.

The intraoral examination reveals changes at the odontal level (increased frequency of carious lesions, at the cervical level of the frontal teeth and at the occlusal faces of the lateral teeth), at the periodontal level (erythematous marginal gingivitis, hyperplastic gingivitis, pregnancy tumor, superficial/deep marginal periodontitis).

Conclusions. Oral changes associated with pregnancy should be known and detected as early as possible in order to improve symptoms and prevent complications in various compartments of the body. Increased attention is required during pregnancy, the approach and therapy in such situations being complex, interdisciplinary, addressing both the body in general and the elements of the stomatognathic system, in order to restore the homeostatic balance.

Keywords: pregnancy, oral cavity, tooth decay, gingivitis

From asymptomatic bacteriuria to septic shock during pregnancy

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Introduction. Urinary tract infections (UTI) are common during pregnancy and can be diagnosed as asymptomatic bacteriuria, acute urethritis, acute cystitis and acute pyelonephritis, which are exceptionally complicated by septic shock. **Materials and method.** From the second half of pregnancy, anatomic and physiological changes can lead to urinary stasis and symptoms associated with urinary tract infections. The management of urinary tract infections during pregnancy is desirable to be as accurate as possible, otherwise it can cause some severe complications, such as acute pyelonephritis, acute renal failure, premature labor, hemolytic anemia, septic shock, intrauterine growth restriction and intrauterine death. We will exemplify each of these entities by presenting eloquent clinical cases. **Results.** Acute pyelonephritis varies between 2% and 9% of all pregnancies, being directly related to the monitoring of pregnant women, an early and correct diagnosis of urinary tract infections, but also to an appropriate and

prompt treatment. Urinary tract infections during pregnancy should be recognized quickly. Always, both the general practitioner and the obstetrician must think that a pregnant woman with isolated or associated clinical signs (fever, low back pain, abdominal pain, dysuria, chills) can have urinary tract infections that can evolve. Asymptomatic bacteriuria during pregnancy should be promptly treated. Also, after 14 days from the end of treatment, the infection should be checked to be negative by repeating urine culture. Urinary tract infections in pregnancy are associated with increased uterine contractions, but also with iron deficiency anemia, which must also be treated (tocolytic therapy, iron supplements). **Conclusions.** The cases presented show that a correct diagnosis and an appropriate treatment are very important. If these two purposes are missed, the evolution can rapidly progress and can be severe for either the fetus or the mother.

Keywords: urinary tract infections, pregnancy

Distribution and pathogens associated with female lower genital tract infection in pregnant and nonpregnant women from Iași city area

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Background. Vaginosis is the most common gynecological problem affecting women of all ages. The aim of the study was to assess the prevalence of vaginosis correlated to pregnancy, the pathogens associated and their resistance pattern. **Materials and method.** This study was conducted in Biodev Medical Center, Iași, Romania, during 2013-2018, where a total of 1480 women with different ages were tested for lower genital tract infections. Vaginal samples (swabs) were taken by gynecologists from all the women who were consulted in this period of time. All vaginal swabs were cultured on special medium and incubated according to the protocol. All the positive samples were isolated, identified and made antibiogram and antifungigram profile. The data were compiled and analyzed for lower genital tract infection, prevalence and distribution of involved pathogens among pregnant and

nonpregnant women, along with the antibiogram and the antifungigram pattern. **Results.** Pregnant women were found with a higher rate of vaginosis (46.43% of the total pregnant women records), mainly fungal vaginosis (83.33%). Nonpregnant women had a lower percentage of vaginosis (35.52%), most of them caused by bacteria (51.93%). The highest antifungal resistance was for fluconazole (28.78%) and itraconazole (27.72%). The highest antibacterial resistance was for ceftioxin and oxacillin (53.31%). **Conclusions.** Pregnancy has an influence on the equilibrium of the vaginal microbiome and can facilitate the onset of vaginosis. The resistance pattern was similar with the one found on previous studies in the literature.

Keywords: vaginosis, genital tract infection, non-pregnant women

Thrombophilia screening – is it useful or not in pregnancy?

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Introduction. Both vein and artery thrombosis with embolic complications is probably the most important cause of morbidity and mortality in developed countries. Thrombophilia can be inherited or acquired. Excessive coagulation activation or inhibition of anticoagulant mechanisms may cause a state of hypercoagulability with the occurrence of thrombosis. It is already known that pregnancy can affect the hemostatic system into a hypercoagulable state. It generally exists a significant change to coagulation, with increased factor VII, VIII, X and von Willebrand factor activity and increases in fibrinogen. The screening for thrombophilia in pregnancy is not routinely recommended in the absence of venous thromboembo-

lism. **Materials and method.** The aim of our study was to identify the prevalence of thrombophilia in a group of women with normal pregnancy outcomes. **Discussion and results.** The most common inherited disorders during pregnancy were mutations in factor V Leiden, prothrombin gene, and methylenetetrahydrofolate reductase (MTHFR). **Conclusions.** Currently, routine screening for thrombophilia defects is not recommended in women without previous pregnancy complications. However, the prevention of complications such as recurrent miscarriage remains a major and topical health issue.

Keywords: thrombophilia, pregnancy, hypercoagulable state

Clinical case: management of HIV infection during pregnancy

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Introduction. The number of pregnant women living with HIV has remained constant during the last years in the Republic of Moldova. It is known that HIV infection, associated with other pathologies, complicates the evolution of pregnancy, requiring a complex approach. HIV infection is often associated with premature birth, fetal growth restriction (FGR), increased perinatal mortality and morbidity rate. **Materials and method.** A 19-year-old pregnant, G2P1, was admitted to the third-level perinatal center of the Institute of Mother and Child, at 37-38 weeks of amenorrhea. High viral load for HIV and multiple fetal abnormalities were detected in a previous pregnancy (2018), presenting an indication for pregnancy interruption. Currently, the patient is receiving antiretroviral therapy (ARVT), with HIV RNA PCR 40<copies/mL, and CD4 count of 1365. Simultaneous conditions were detected: *Trichomonas vaginalis* infection, chronic viral hepatitis B, epilepsy without treatment for four years, and mental retardation. **Results.** Fetal cardiotocography determined a monotonous path with a tendency to

bradycardia (basal rate ≤ 100 beats/min), also the ultrasonographic examination detected FGR (fetal biometric parameters <3rd percentile) and oligoamnios (amniotic fluid index ≤ 3 cm); reverse flow and velocimetry pathological Doppler flow on the fetal middle cerebral artery. In fetal interest, an emergency caesarean section was performed. A 2100 g fetus, Apgar 7/8 score, was extracted. The patient continued the administration of ARVT, along with antibiotic therapy. The newborn received ARVT, being artificially fed. **Conclusions.** The complex approach and the adequate management of the perinatal period in a patient with HIV infection require the assessment of the viral load for HIV, ARVT associated conditions and their influence on the fetal state. An important aspect consists in the decision about the modality and the time of delivery, according to maternal/fetal indications, and the artificial feeding of the newborn, in order to reduce the possible complications.

Keywords: HIV, viral load, fetal growth restriction, antiretroviral therapy

16P11.2 deletion syndrome – case report

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We present the case of a suspicion of 16p11.2 deletion syndrome, undiagnosed by amniocentesis and PCR testing because the deletion of the 11.2p sequence was diagnosed only by genetic analysis SNP array performed at 10 months of age. In the absence of lethal fetal abnormalities, the couple did not want additional micro array testing at the time of antenatal suspicion of a genetic syndrome, a sus-

picion based on severe symmetrical fetal restriction at the time of routine fetal anomaly ultrasound. Fetal anomaly scan in the second trimester raises the suspicion of a fetal genetic syndrome by following the standardized protocols, corroborated with the medical and obstetric history.

Keywords: 16p11.2 deletion syndrome, genetic analysis

Transplacental transmission of hepatitis C virus infection

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Introduction. Vertical transmission of hepatitis C virus (HCV) occurs in rare cases (5-8%), more often during birth and, seldom, transplacental, before birth. Hepatitis C virus can cause acute or chronic hepatitis. **Materials and method.** We present the case of a 42-year-old woman, gravida 2, para 2, with 32 weeks of gestation. The ultrasound exam noticed fetal ascites, polyhydramnios and echogenic fetal bowel. The mother was tested for the TORCH panel, including HCV. Anti-HCV antibodies were present. We decided to perform fetal cordocentesis, paracentesis and amniocentesis. From cordocentesis we obtained approximately 8 ml of fetal blood, analyzed for: albumin, direct bilirubin, indirect bilirubin, total bilirubin, blood count, blood glucose, direct Coombs test, HCV RNA, IgM antibodies for cytomegalovirus/toxoplasmosis/Rubella/herpes simplex type 1 and 2. Also, 160 ml of fetal ascites fluid were sent for cytological and biochemical analysis, and 40 ml of clear amniotic fluid were used to detect infection with herpes simplex, Epstein-Barr or parvovirus. **Results.** The biochemical

tests and blood count performed from the fetal blood were within normal range. The direct Coombs test was negative. HCV RNA was detected. Antibodies for cytomegalovirus/toxoplasmosis/Rubella/herpes simplex type 1 and 2, Epstein-Barr and parvovirus B19 were absent. The biochemical tests performed from the fetal ascites fluid showed: red blood cells 3000/mm³, leukocytes 835/mm³, glucose 57 mg/dL, albumin 1.90 g/dL, creatinine 0.53 mg/dL, urea 19 mg/dL, proteins 3.4 g/dL, positive Rivalta test. HCV RNA was detected. IgM antibodies for cytomegalovirus/toxoplasmosis/Rubella/herpes simplex type 1 and 2 were all absent. Fetal ascites markedly decreased and normal echogenicity of the bowel was noted. **Conclusions.** In rare cases, HCV can be transmitted vertically from the mother to the unborn baby. Cordocentesis and paracentesis helped us diagnose the fetus before birth and improve his prognosis after birth.

Keywords: ascites, HCV infection, cordocentesis, paracentesis, amniocentesis

Lymphadenectomy in gynecological malignancies

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Lymphadenectomy is an integral part of the surgical treatment of gynecological cancer, being used for staging and regional tumor control. Surgical anatomy: anatomical spaces and planes, vascular, ureteral, lymphatic and nervous anatomy. Principles: define clear anatomic landmarks, en-bloc resection along with vessels and nerves, avoid morcellation, avoid the use of monopolar current close to the nerves. **Indications of pelvic lymph node dissection.** 1) Cervical cancer – T1a1 (considered in T1a1 LVSI-positive), T1a2 (considered in LVSI-negative, performed in LVSI-positive, Ia2 – IIa FIGO, pelvic exenteration). 2) Endometrial cancer – low risk (G1 or G2 + myometrial invasion <50%) – not recommended, intermediate risk (G1 or G2 + myometrial invasion >50% or G3 + myometrial invasion <50%) – considered for staging purposes in these patients, high risk (G3 + myometrial invasion >50%) – recommended. 3) Ovarian cancer: early stages (I-II), advanced stages (III) – optimal procedure. 4) Vulvar cancer – enlarged

(>2 cm) pelvic N are identified – their removal should be considered. **Indications of lombo-aortic lymph node dissection.** 1) Ovarian cancer – early stages, advanced stages (optimal procedure). 2) Cervical cancer: stages Ia2 – IIa SLN+, advanced stages (staging). 3) Endometrial cancer – stage I (intermediate and high risk), stages IIa-IIIa. **Indications of inguinofemoral lymph node dissection:** vulvar cancer T>T1a, unifocal T<4 cm, groin N0 (clinical examination and imaging) – SLN; T≥4 cm and/or multifocal invasive disease, inguinofemoral lymph node dissection by separate incisions; lateral T (medial border >1 cm from midline), ipsilateral inguinofemoral lymph node dissection; contralateral inguinofemoral lymph node dissection – when ipsilateral nodes show M disease. Superficial and deep femoral N should be removed. The preservation of the saphenous vein is recommended.

Keywords: sentinel lymph node biopsy, excision of only bulky nodes, pelvic lymph node sampling, complete (systematic) pelvic lymphadenectomy

HPV infection – a potential cause for fetal-maternal morbidity?

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Introduction. Human papillomavirus (HPV) is the most common sexually transmitted infection in women at reproductive age. Its implication in the development of cervical carcinoma is undisputable but, more so, during the last decades, it has been shown that HPV infection could also have an impact on the outcomes of pregnancies. **Methodology.** We researched PubMed, UpToDate, Wiley databases and online journals, analyzing relevant clinical trials and reviews published after 2000 regarding the effects of HPV infection on the pregnancy outcomes. **Discussion.** Throughout the years, studies showed that HPV infection could lead to premature birth as a result of

preterm prelabor rupture of membranes (PPROM), prelabor rupture of membranes (PROM), neonates with lower Apgar score, infectious complications and higher neonatal mortality rates. Studies show that mostly the persistent HPV infection with high-risk genotypes and previous treatment for CIN were associated with even greater risks regarding pregnancy outcomes. **Conclusions.** The inconsistencies found during our research have led to the conclusion that there is a necessity for larger homogenous studies. Also, the focus of the medical community towards HPV vaccination programs remains a priority.

Keywords: HPV infection, premature birth, PPRM

The risk of placental thrombosis associated to the infection with SARS-CoV-2

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Introduction/objective. The infection with SARS-CoV-2, after approximatively two years from its debut, continues to be a major public health problem, not only due to the high number of new cases admitted to intensive care unit, but also due to the number of deaths recorded on a global level. The pregnancy has been reported to be an independent risk factor in respect to the side effects associated to the infection with SARS-CoV-2, especially in the case of pregnant women with associated pathology, such as gestational diabetes or preeclampsia. More reports have pointed to a high risk of placental lesions, caused by hypoperfusion and inflammation of women infected by SARS-CoV-2. The eventual association between the infection with SARS-CoV-2 and the affliction of placental functionality are crucial, because they could lead to fetal decompensation and to an implicitly greater risk of perinatal mortality. **Methodology.** We searched and analyzed the articles published in the specialized literature in order to evaluate the risk of placental thrombosis associated

with SARS-CoV-2. **Results.** The majority of the studies have reported the presence of maternal vascular malperfusion in a proportion of approximatively 30% in the cases of the analyzed patients infected with SARS-CoV-2. At the same time, fetal vascular malperfusion has been observed in 27% of the studied cases. As a histopathological mechanism, the perivillous fibrin growth has been reported in proportion of 32%, while intervillous thrombosis has been observed in 14% of the cases. **Discussion and conclusions.** A significant proportion of placentas have presented histopathological modifications, suggesting hypoperfusion and placental inflammation amongst pregnant women infected by SARS-CoV-2. Nonetheless promising, the available evidence is based on a restricted number of clinical studies. Therefore, multicenter prospective blinded studies are needed in order to correlate these placental lesions to the pregnancy results.

Keywords: placental hypoperfusion, thromboembolic risk, SARS-CoV-2

New treatment options in urogenital atrophy

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Introduction/objective. Vaginal atrophy is a disease associated with menopause caused by a definite decrease in ovarian hormones, with a negative impact on patients' quality of life. Systemic and local hormone replacement therapy is the current treatment for vaginal atrophy. The adoption of new long-term therapeutic strategies such as injection of materials into the vaginal wall (platelet-rich plasma [PRP], autologous fat graft [AFG], hyaluronic acid [HA], botulinum toxin [BTX] and collagen) is an alternative therapy, in order to suppress the painful symptoms and to control the other symptoms associated with vaginal atrophy. **Methodology.** We performed a search and analysis of articles published in the literature to evaluate new treatment options in vaginal atrophy and the rate of suppression of symptoms. **Results.** The effectiveness of treatment in vaginal atrophy is currently limited. Therefore, it is necessary to explore new therapeutic strategies to minimize the adverse effects of

the current hormonal treatments. Recently, two studies in the literature demonstrate the role of regenerative medicine in the local treatment of urogenital atrophy by single local injection of autologous microfragmented adipose tissue. This could be a new viable solution for these patients, as it not only helps to relieve symptoms, but also counteracts the mechanisms that lead to menopausal genitourinary atrophy. **Discussion and conclusions.** Although promising, the available evidence is based on a limited number of well-conducted clinical trials. Therefore, properly constructed clinical trials are required to obtain more conclusive results on the promising role of autologous and microfragmented adipose tissue as a safe, feasible and effective therapeutic approach for the treatment of postmenopausal urogenital atrophy.

Keywords: vaginal atrophy, menopause, adipose tissue

Minimally invasive surgery for apical prolapse

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Introduction. Symptomatic pelvic organ prolapse has a relatively high prevalence and women have a 13-20% lifetime risk of having a surgical procedure to repair vaginal support defects. Despite the anterior vaginal compartment being the most common site of pelvic organ prolapse, the loss of apical support is typically associated with defects that usually occur at the insertions of cardinal-uterosacral ligament complexes, pubocervical fascia, and rectovaginal fascia to the pericervical ring. In addition to the midline defects in the posterior vaginal wall, detachments of the rectovaginal fascia along the arcus tendineus fasciae rectovaginalis and breaks at the pericervical ring insertion are responsible for the lateral and transverse defects, respectively. All of these defects can form rectoceles. Minimally invasive pelvic surgery to correct apical prolapses and posterior defects primarily includes laparoscopic or robotic assisted hysterectomy-/sacrocolpopexy for defects that are more than grade III (grade III and IV) and the native tissue alternative of uterosacral ligament culdoplasty and suspension for defects that are less than grade III (grade II or III). **Materials and method.** In this paper, we present several cases of pelvic organ prolapse through which we highlight the techniques and advantages of the minimally invasive

pelvic reconstructive surgery. **Results.** The gold standard procedure for apical prolapse that are grade III or IV remains the sacral colpopexy that suspends the vaginal vault by reinforcing the anterior and posterior vaginal fibromuscularis with mesh secured to the anterior longitudinal sacral ligament. The laparoscopic or robotic repair techniques of a uterine or vaginal vault prolapse or a rectocele that are grade II or III must address the reconstruction of the pericervical ring and its attachments to the cardinal-uterosacral ligament complexes, pubocervical fascia, and rectovaginal fascia by approaching the uterosacral ligaments together and reattaching to these ligaments. **Conclusions.** Sacrocolpopexy is the gold standard repair for apical prolapse that are grade III or IV for those who desire to maintain their sexual function, and minimally-invasive approaches offer similar efficacy with fewer risks than open techniques. Laparoscopic or robotic uterosacral ligament culdoplasty and suspension with reinforcing of the pericervical ring is a safe and effective native tissue option for grade II or III defects.

Keywords: apical prolapse, robotic surgery, laparoscopic surgery, sacral colpopexy, uterosacral ligament suspension

The value of weight gain during pregnancy on the evolution of delivery

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Introduction. Weight gain during pregnancy is a physiological condition of the expectant mother to ensure good fetal development and to prepare her own body for breastfeeding. But if the weight gain in pregnancy is either low or increased, all the benefits turn into maternal and fetal risk factors. **Materials and method.** A retrospective study was performed, in which 110 medical records were analyzed. **Results.** The mean age of women in study was 31.3 ± 0.8 years old. The mean of gestational weight gain was 15 ± 1.9 kg, and the interval of weight gain was 4 to 27 kg. The average term of gestation at the time of birth was 37.2 ± 0.6 weeks. The birth occurred at less than 37

weeks in 36.3% of pregnant women. Delivery ended with a caesarean section in 27.2% of cases, of which in 60% emergency interventions were performed. In all women who gained more than 20 kg, the birth was complicated by a placental defect. Women with weight gain above the norm were in hospital 1.3 ± 0.6 days longer. **Conclusions.** Weight gain is one of the few things that we can control prophylactically during pregnancy. We must be aware that the rate of obstetric success depends on the nutritional status of the mother. Women with weight gain above the norm have more risk factors and need longer medical care.

Keywords: weight gain, pregnancy, birth

The impact of glypressin in laparoscopic myomectomy

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Introduction. A large-scale myomectomy-associated issue to be noticed in this respect is extreme blood loss. The aim of the current study was to assess the effect that glypressin has on blood loss while the procedure of laparoscopic myomectomy (LM) is performed on women diagnosed with uterine myomas. **Materials and method.** An observational study was conducted at the "Cuza Vodă" Clinical Hospital of Obstetrics and Gynecology, Romania. Our unit is a tertiary referral center for advanced laparoscopic gynecological procedures in Northeastern Romania. Data were collected from 188 patients, between 23 and 54 years old, who underwent LM at our department from January 2013 to December 2019. Then, to the first group of women (n=64) was given a 5-ml intramyometrial injection of glypressin 0.2 mg/ml (glypressin group; Group 1), while the second group of women (n=124; Group 2) had an LM performed without any other method aiming to re-

duce blood loss. **Results.** The decreases in postoperative hemoglobin (Hb), hematocrit (Ht), morbidity and duration of hospital stay were assessed. The resulting clinical data revealed that Hb and Ht (as it was presumed) featured similar changes in our study. Statistically significant differences ($p < 0.05$) were drawn out from the two groups in relation to Hb and Ht; after LM, both Hb and Ht were decreased. **Conclusions.** Glypressin has made it possible to perform beneficial and rapid uterine reconstruction with reduced blood loss during LM. Glypressin has been revealed to be effective in reducing blood loss during LM. In the present study, the use of a dilute solution was associated with no side effects. Blood loss remains an issue in most cases operated without the aid of a vasoconstrictor agent. In addition, the use of this synthetic analogue helps preserve fertility without a negative impact on pelvic blood supply.

Keywords: glypressin, laparoscopic myomectomy

Research on myoma in Northeastern Romania and socio-medical outcomes

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Introduction. Myomas represent the most widely encountered benign uterine tumors in women of childbearing age, with an occurrence of up to 77% and a dominant impact on the women’s state of health. The aim of our study was to provide the necessary information with reference to the incidence and prevalence of myomas in the patients admitted to a tertiary referral center in Northeastern Romania. **Materials and method.** This retrospective study conducted at the “Cuza Vodă” Clinical Hospital of Obstetrics and Gynecology, Iași, Romania, comprised 11,538 patients, representing all the patients hospitalized at the gynecology department between January 2013 and December 2019. **Results.** During the interval of the study, the number of hysterectomies (total and for myomas) has increased. What is to be noticed is the fact that the rate of laparoscopic surgery revealed a small decrease (31.3% from 34%), the classic therapy showed a decrease by more than 10%, and the hysteros-

copy rate tripled. One cannot state that there are many studies in the medical field that have established with accuracy the incidence of these myomas. In the current study, the prevalence of hysterectomy for myomas was 54.42%. Our results are in agreement with the data from other medical studies, namely that a percentage of 40-60% of all performed hysterectomies are for myomas. **Discussion.** Uterine myomas remain the most common diagnosis among women admitted to our hospital. It is very important for the practitioner to understand the physical and psychological needs of these patients. Because many patients consider the uterus as a sexual organ, as a symbol of one’s fertility, the surgeon must fathom its importance. This is the main reason why after hysterectomy most patients suffer an emotional trauma, with a decrease in self-esteem, anxiety and depression.

Keywords: myoma, hysterectomy, laparoscopic surgery

Genital infection with *Ureaplasma urealyticum* and pregnancy impact

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Introduction. Chorioamnionitis – or intraamniotic infection – is the infectious process that affects intrauterine content during pregnancy. Numerous studies reported vaginal colonization with different types of infectious agents as a risk factor for chorioamnionitis. Although this complication occurs due to the ascending polymicrobial bacterial infection at the time of membrane breakage, it may also occur in pregnant women with intact membranes, mainly due to *Ureaplasma urealyticum* and *Mycoplasma hominis*. **Aim.** We tried to identify our regions specific panel of infectious agents that determine more frequently premature birth and premature rupture of membranes (PROM). **Materials and method.** We conducted a 10-year retrospective study in the “Cuza Vodă” Clinical Hospital of Obstetrics and Gynecology from Iași.

We included 1301 pregnant women with PROM and premature birth or spontaneous abortion. **Results.** We noticed that the main infectious agent is different in our five groups. The distribution varies also depending on the environment. The most frequent germ present in the vaginal cultures of the pregnant women enrolled in our study, regardless of the gestational age, is *Ureaplasma*. **Discussion and conclusions.** This may suggest the need for new studies confirming that the diagnosis and treatment according to the antibiotic resistance of vaginal infections for *Ureaplasma urealyticum*/*Mycoplasma hominis* in the first trimester of pregnancy could prevent premature birth, abortion or chorioamnionitis.

Keywords: genital infection, *Ureaplasma urealyticum*, *Mycoplasma hominis*, chorioamnionitis

PRP (platelet-rich plasma) in infertility

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Introduction. Platelet-rich plasma (PRP) is an innovative solution in female infertility, representing a new treatment model for the thin endometrium. PRP is a biologic therapy with no side effects, as it is prepared from the patient's blood and contains many growth factors and cytokines, such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor (TGF) and many other cytokines that can facilitate tissue regeneration and healing. **Materials and method.** The endometrial rehabilitation technique with PRP has been performed in 78 patients with infertility, aged between 23 and 45 years old. **Results.** Intrauterine infusion with PRP stimulated and accelerated the growth of the endometrium (100%), decreased fibrosis, thus decreasing intrauterine adhesions in women with Asherman syndrome, decreased

sperm inhibition in endometrial secretion, determining the success of embryo implantation in six cases: two pregnancies by *in vitro* fertilization, of which one twin pregnancy after an IVF failure and another after five previous IVF failures, three spontaneous pregnancies and one ectopic pregnancy. **Conclusions.** Intrauterine PRP treatment increases the rate of pregnancy in infertile women with thin endometrium, as it increases the receptivity and vascularity of the endometrium because it contains growth factors that have positive effects on local tissue repair and endometrial receptivity. PRP has a positive impact on the increase in the number of antral follicles and prevents the inhibition of sperm in the peritoneal tubal fluid. PRP is an alternative for women with low follicular reserve and thin endometrium who still want a pregnancy.

Keywords: PRP, endometrium, IVF, infertility

The influence of SARS-CoV-2 infection during pregnancy

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Introduction. At the early stage of the coronavirus disease 2019 (COVID-19) pandemic, most studies reported that very few pregnant women developed severe forms of the disease; however, recent data indicate that they may face severe morbidity and mortality. Although the pregnant population was affected by early waves of the COVID-19 pandemic, increasing transmission and severity due to new viral variants has resulted in an increased incidence of severe illness during pregnancy in many regions. Critical illness and respiratory failure are relatively uncommon occurrences during pregnancy, and there are limited high-quality data to direct management. **Materials and method.** The guiding question was: "What evidence is available in the literature about the clinical and obstetric aspects of SARS-CoV-2 infection during pregnancy?" **Results.** From the time of

the reports of the first cases of COVID-19 in late 2019, much has been learned about the effects of SARS-CoV-2 infection during pregnancy. However, many questions remain. Pregnancy increases the risk of severe disease associated with COVID-19, but whether pregnant persons are more susceptible to infection is unknown. **Discussion and conclusions.** Most experts believe that SARS-CoV-2 is likely to become endemic. Thus, the continued collection of data on the effects of SARS-CoV-2 infection during pregnancy and the effects of COVID-19 vaccines are needed. Therefore, it is essential that we maximize the lessons learned from the COVID-19 pandemic so that they can be applied to improve our planning and response to emerging infections in the future.

Keywords: coronavirus infections, COVID-19, pregnancy, pregnancy complications

Bowel endometriosis – Bucharest endometriosis center experience

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Introduction. Endometriosis is a chronic, inflammatory, estrogen-dependent condition which affects approximately 10-15% of reproductive-aged women. Affecting up to 37% of women with endometriosis, bowel endometriosis is the most common site for extragenital endometriosis and may present as deep dyspareunia, dyschezia, diarrhea or constipation, bloating, blood in the stool, pain with sitting and chronic pain. We present our four-year experience conducted in the Bucharest Endometriosis Centre, which proudly gathers multiple laparoscopic specialists who provide patient-targeted multidisciplinary treatment of bowel endometriosis. **Methodology.** Our team consists of three gynecologists, two general surgeons, one urologist, one consultant radiologist and five ART (assisted reproduction technique) specialists. In four years, we managed 912 endometriosis cases in women with ages between 14 and 52 years old. All surgeries were done laparoscopically. **Results.** Among all our cases, 662

patients proved to have deep infiltrating endometriosis and 340 patients had bowel endometriosis. We emphasize the chosen types of excision, their location and association pattern of the lesions, along with the intraoperative incidents and complications. **Discussion and conclusions.** The benefits of excisional surgery are undeniable, including not only pain relief, but improvement of the quality of life, potential increase of fertility and cancer prophylaxis. The surgical approach of the bowel endometriosis split into three categories: shaving, disc resection and segmental resection. Based on our extensive experience in conjunction with constant reviewing of the literature, we strongly advise that bowel endometriosis should be managed only by a multidisciplinary endometriosis-specialized team, who is able to diagnose and treat it accordingly, in a minimally invasive fashion.

Keywords: bowel, endometriosis, laparoscopic surgery

Maternal death related to COVID-19

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Introduction/objective. The international literature refers to the negative impact of the COVID-19 pandemic on the poverty, birth and health of the newborn. The aim of the study is to analyze the causes and pathophysiological context of deaths among pregnant women infected with SARS-CoV-2. **Methodology.** The pseudonymized maternal mortality files from 2020-2021 will be analyzed, based on a medical-social evaluation grid. The evolution of maternal mortality in the years of the COVID-19 pandemic compared to previous years will be evaluated, and medical and social factors associated with maternal mortality in pregnant women with SARS-CoV-2 will be discussed. **Results and discussion.** The study results will be presented in terms of data from the literature. Two-dimensional interrelationship of COVID-19 pregnancy will be discussed in terms of

the influence of pregnancy on the COVID-19 evolution and that of SARS-CoV-2 infection on pregnancy. The role of the associated pathology, such as obesity, hypertension or chronic diseases, on the negative outcome of pregnancy, leading to death, will be evaluated. An important aspect of the analysis is the inclusion of the inequalities' indicators studying the influence of the socioeconomic and educational factors in the care of the pregnant woman. **Conclusions.** The conclusions of the study refer to the methods of improving the interventions which tackle the care of the pregnant women in case of infectious epidemic risk, as well as the management of women's health during the fertile period, actions initiated preconceptionally, prenatal, intra- and postnatal.

Keywords: pregnancy, COVID-19, morbidity, death

Ovarian pregnancy – case presentation

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Ectopic pregnancy defines the implantation of the embryo anywhere outside the uterine cavity and is the most common medical and surgical emergency in the gynecological field. The extrauterine implantation of the fertilized ovum in the ovary is rare (0.3-3% of the ectopic pregnancies) and the early diagnosis of this pathology represents a medical challenge due to the nonspecific clinical aspects compared to a tube pregnancy and to the lack of visible gestational sac. We present the case of a 30-year-old patient who presented in our clinic with moderate metrorrhagia which debuted three days before, three weeks and five days of amenorrhea, and with beta-

HCG test in dynamics suggestive of an ectopic pregnancy. The transvaginal ultrasound identified the presence of a formation with mixed echogenicity undifferentiated of the left ovary and a 4-mm endometrium, without fluid lamina in the pouch of Douglas. Laparoscopy was performed and a left ovarian pregnancy was identified, subsequently confirmed by histopathological examination, with a favorable postoperative outcome. Thus, minimally invasive surgical technique remains the gold standard for early diagnosis and treatment in case of ovarian pregnancy.

Keywords: ectopic pregnancy, ovarian pregnancy

Laparoscopy, *in vitro* fertilization and endometriosis

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Laparoscopic surgery can improve pregnancy rates not only for minimal and mild disease, but also for more advanced endometriosis. There is one reason why laparoscopic surgery is less commonly employed today than it has been in the past: higher success rates with *in vitro* fertilization (IVF). Therefore, IVF would seem to be a preferable alternative to repeat surgery for most patients. We suggest to treat large endometriomas of more than 3 cm, especially if the response to ovarian stimulation drugs is poor before surgery. However, such surgery can be very difficult and requires a talented surgeon in order to avoid vascular and ovarian injury that might result in even poorer ovarian response postoperatively. The decision to operate is not easy. We report the increased diagnostic accuracy of laparoscopy in endometriosis us-

ing indigo carmine. The optimal approach to managing the infertile endometriosis patient is to perform a comprehensive evaluation, and then develop a treatment plan that progresses from simpler, yet effective and safe, treatments to more complex and costly treatments. The major advantage of IVF is the fact that it treats multiple infertility problems of both the female and male, has a high rate of success on just one attempt relative to surgery, and takes only 2-3 months to complete the treatment, making it more attractive for older patients. We believe that the subset of patients who have failed multiple cycles of IVF may harbor a certain type of endometriosis which allows them to benefit from a thorough surgical therapy.

Keywords: laparoscopy, *in vitro* fertilization, endometriosis

The uterine microbiome in reproductive medicine

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Technical advances in massive parallel sequencing have allowed the characterization of the whole reproductive tract microbiome in all the compartments beyond the vagina. Because embryo implantation occurs in the uterine cavity and not in the vagina, reproductive medicine remains primarily interesting in the endometrial microbiota and their impact on pregnancy establishment and maintenance. Molecular identification of bacterial species using 16S rRNA-targeted polymerase chain reaction has allowed the detection of at least one of the 12 surveyed bacterial taxa in 95% of the endometrial samples. The role of endometrial microbiota at the embryo-maternal interface in the onset of pregnancy is of great interest in reproductive medicine. The reproductive outcome was consistently poor upon isolation of endometrial pathogens compared with cases with negative culture. The isolation of *Lactobacillus* spp. was associated with increased implantation and pregnancy

rates per transfer and with lower miscarriage rates. A clear scenario of altered endometrial microbiota is chronic endometritis, the persistent inflammation of the uterine lining mainly caused by bacterial pathogens. Because it is often asymptomatic, chronic endometritis is seldom suspected and diagnosed, leading to important inconsistencies in the estimated prevalence reported for this disease. We suggest that antibiogram-driven treatment of chronic endometritis in repeated implantation failure or recurrent pregnancy loss patients improves their reproductive outcomes. The endometrial microbiome seems to have an impact on embryo implantation and pregnancy maintenance, as an altered endometrial microbiome, characterized by a low abundance of *Lactobacillus*, has been associated with implantation failure and pregnancy loss.

Keywords: uterine microbiome, reproductive medicine

COVID-19 severe pneumonia in a pregnant patient with quadruplets – case report

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The multiple pregnancies associated with COVID-19 represent a new and difficult condition to manage. The prognosis for rapid deterioration after caesarean delivery is difficult to assess and needs close interdisciplinary follow-up due to pregnancy and postpartum-related changes. We report the case of a 37-year-old primigesta, primipara patient who was admitted to the “Elena Doamna” Clinical Hospital of Obstetrics and Gynecology, Iași, at 33 weeks and 3 days of gestation with high-grade multiple pregnancies (quadruplets) for threatened premature birth associated with COVID-19. The patient had a history of surgically corrected atrial septal defect during childhood and is currently known to have paroxysmal supraventricular tachycardia. Tocolysis was ineffective and the decision to perform a caesarean operation was made. The diagnosis was established: primigesta, primipara, at 34 weeks of gestation, high-grade multiple pregnancy with quadruplets, intact membranes, threatened

premature birth, surgically corrected atrial septal defect, paroxysmal supraventricular tachycardia, infection with SARS-CoV-2. The patient underwent a caesarean intervention and treatment for COVID-19 pneumonia. The intervention took place at 33 weeks and 4 days of gestation, resulting in four newborns with weight between 1400 g and 1820 g and Apgar scores between 6 and 8. All newborns were transferred to a third-degree neonatology ICU service due to their prematurity. During the postpartum period, the patient had a fulminant evolution of COVID-19 pneumonia, with rapid deterioration, needing respiratory support and antiviral treatment with remdesivir. Managing high-risk obstetrical pregnancies associated with COVID-19 requires a multidisciplinary team consisting of obstetricians, anesthesiologists, neonatologists and infectious disease specialists.

Keywords: quadruplets, postpartum pneumonia, COVID-19 pneumonia

Laparoscopy as a triage test for resectability in advanced ovarian cancers

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Ovarian cancer is a major public health problem, ranking fifth in cancer incidence and fourth regarding the specific cause of death for women. It accounts for 5% of all cancer deaths. More than two-thirds of ovarian cancers are diagnosed in advanced stages due to the lack of specific symptoms and adequate screening methods. The diagnostic evaluation of a woman suspected to have an ovarian cancer is based on clinical examination, ultrasonography, CT scan of the abdomen and pelvis and serum markers (CA 125). The standard treatment of ovarian cancer is primary cytoreductive surgery followed by taxanes- and platinum-based chemotherapy. The most important prognostic factor in the treatment of ovarian cancer is the residual tumor volume after surgery. The best results are registered when there is no visible residual tumor or when residual tumor is less than 0.5 cm. The success of the of the primary cytoreductive surgery depends on the skill of the gynecologic-oncology surgeon, the patient's status and the extensiveness of the disease. Clinical and imaging methods for diagnosis are not the best tools to evaluate the resectability of the disease. Traditionally, laparotomy was used to evaluate

the surgical staging. When the disease was considered unresectable, three cycles of chemotherapy were delivered (neoadjuvant chemotherapy; NACT) and followed by interval debulking surgery with the aim to perform an optimal cytoreductive surgery. Today, laparoscopy is considered as a triage test to decide if the treatment will start with primary debulking surgery or NACT. A recent Cochrane Database of Systematic Reviews showed no conclusive data on laparoscopy to evaluate the extensiveness of the disease and predict its resectability. Many oncology centers use the triage test as a standard protocol and many clinical trials were conducted with the aim to reduce the high morbidity associated with primary surgery in advanced disease and to know if survival is the same comparing primary surgery with NACT and interval debulking surgery. The Department of Gynecologic Oncology of the "Filantropia" Clinical Hospital of Obstetrics and Gynecology, Bucharest, uses triage laparoscopy to select advanced cases of ovarian cancer for primary cytoreductive surgery or NACT followed by interval cytoreductive surgery.

Keywords: ovarian cancer, laparoscopy

Placenta – the key witness of COVID-19 in pregnancy?

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Introduction. The protective role of the placental barrier to bacterial and viral infections, the immune tolerance of the fetus still represents a medical challenge and subject of research. The impact of COVID-19 in pregnancies is continuously discussed especially because COVID-19 maternal infection has been the cause for unfavorable pregnancy outcomes. **Materials and method.** We performed database research with the terms: "COVID-19", "placenta", and "pathology" in PubMed, Embase, Scopus, ScienceDirect, Web of Science and Cochrane. **Results.** The research revealed 457 results. Even though there are published numerous reports, the effect of SARS-CoV-2 on the developing fetus remains unclear. Most publications admit that vertical transmission is unusual; but there is evidence

that placental and fetal infection may occur. Placentas from patients with COVID-19 are inflammatory, thrombotic, and vascular changes that have been found in other inflammatory conditions. Peculiar lesions such as chorangiosis were identified. It may be considered that the inflammatory impact of SARS-CoV-2 infection during pregnancy could justify adverse obstetrics and neonatal events. The impact of vaccine against SARS-CoV-2 on placental represents another subject of debate. **Conclusions.** This presentation will expose the known literature and self-experience about the placenta in SARS-CoV-2 infection and possible outcomes of prenatal exposure to the virus.

Keywords: SARS-CoV-2 infection, COVID-19, placenta

The neonatal consequences of intrauterine infection – herpes simplex virus and Epstein-Barr virus in pregnancy

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Introduction. Herpes simplex (HSV) and Epstein-Barr (EBV) viruses are widespread infections within human population, with over 80% adults being infected during their lifetime, both being reactivated under psychological stress and immunocompromised state. HSV is estimated to affect around 2-3% of pregnancies and newborns with congenital HSV can develop serious consequences such as central nervous system and ocular diseases. On the other hand, EBV rate in pregnancy is extremely low, especially due to lack of primary screening tests, and it is stated that congenital abnormalities may occur in case of fetal infection. This review covers the importance of HSV and EBV infections in pregnancy along with neonatal consequences, diagnostic approaches and therapeutic management. **Methodology.** We selected the studies from PubMed database and reviewed articles from literature, aiming to evaluate and analyze data about HSV and EBV infections in pregnancy and their neonatal outcomes. We included systematic reviews as well as clinical trials and theoretical studies. Our re-

search included all the publications during the period of January 2000 to April 2022 using the following Medical Subject Headings: “HSV”, “EBV”, “pregnancy”, “placental infection”, “neonatal outcomes”. **Results.** Regarding HSV infection during pregnancy and the neonatal outcomes, the evidence that supports a direct relation to specific diseases is mounting, taking into consideration that HSV screening is performed at the onset of the pregnancy more often due to its related known complications. Based on our findings, there are few publications on the outcome of EBV infection in neonates and most of them imply a low rate of congenital disease compared to control groups; however, there are major abnormalities that should be mentioned, such as ventricular sept defect and hydrocephalus. **Conclusions.** Further prospective studies with large number of patients with active or recurrent HSV/EBV infection are needed in order to identify a possible disease pattern in infants related to these viruses.

Keywords: intrauterine infection, herpes simplex virus, Epstein-Barr virus, pregnancy

Probiotic interventions to reduce group B *Streptococcus* colonization in pregnancy – literature review

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Introduction/objective. Worldwide, group B *Streptococcus* (GBS) colonizes up to 15-40% of pregnant women, being the leading cause of neonatal infections in developed world, hence the efforts to primary prevent the antepartum GBS infection are of high interest for healthcare providers. Around 50% of neonates born to GBS-positive women will become colonized with GBS and 1-2% will develop early-onset group b *Streptococcus* disease (EOGBSD). The background of this paper consists of the studies that prove the fact that pregnant women with high colonization of *Lactobacillus* are more likely to have no detectable vaginal GBS, therefore the question remains: “Is it possible to prevent or to decrease GBS colonization by supplementation of probiotics?”. **Methodology.** We selected the studies from PubMed and Google Academics databases and reviewed articles from literature, aiming to evaluate the probiotic effects on pregnant women with GBS and its outcomes. We included systematic reviews and meta-analyses as well as clinical trials and theoretical studies. Our research included all the publications during the period

of January 2004 to April 2022 using the following Medical Subject Headings (MeSH): “probiotic”, “group B *Streptococcus*”, “antenatal”, “pregnancy”, “colonization”, “bacterial vaginosis”, “*Lactobacillus*”. **Results.** Most of the studies concluded that probiotic interventions appear to be a safe and cost-effective primary prevention for GBS-positive women; however, there are some limitations regarding the dosage, the intervention time and different probiotic strains. **Discussion and conclusions.** In countries where antenatal GBS screening is used, the application of this low-risk intervention can reduce the need for intrapartum antibiotic prophylaxis, but further studies need to be conducted for greater significance. The purpose of this paper is to present an insight of recent theoretical papers and to meta-analysis studies of the efficacy of the probiotics administrated to reduce GBS colonization in pregnancy and its postpartum consequences.

Keywords: probiotic, group B *Streptococcus*, antenatal, pregnancy, colonization, bacterial vaginosis, *Lactobacillus*

Parvovirus B19 infection – harmless virus or pregnancy threat?

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Introduction. Parvovirus B19 (B19V) is the causative agent of the relatively benign childhood disease erythema infectiosum (fifth disease). Maternal B19V infection can lead to serious fetal complications during pregnancy. Up to 50% of women are nonimmune and susceptible to B19V infection. **Methodology.** We studied the literature and we search for the most frequent complications that were reported in the European Union regarding the parvovirus B19 infection. **Results.** Infection may result in anemia, spontaneous abortion and/or hydrops fetalis.

The early diagnosis of B19V infection will identify those at risk and may allow for early intervention therapy, thereby improving fetal survival. The virus is spread *via* aerosol droplets through the respiratory route. It can be spread transplacentally to the fetus during active maternal infection (33% transmission rate across the placenta). **Conclusions.** Most pregnant women are asymptomatic but, for an appropriate patient management, there is a need for an accurate B19V diagnosis.

Keywords: infection, B19 parvovirus, hydrops

Isthmocele: curing a major surgery complication with minimal invasive techniques

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Introduction. An isthmocele, a caesarean scar defect or uterine niche, is any indentation representing myometrial discontinuity or a triangular anechoic defect in the anterior uterine wall, with the base communicating to the uterine cavity, at the site of a previous caesarean section scar. **Methodology.** We studied the literature and we analyzed international standards of treatment regarding this defect and the criteria which are important for the treatment algorithm. **Results.** The hysteroscopic resection of isthmocele is a minimally invasive, non-time-consuming and low-morbidity procedure, allowing visualization and repair of the defect.

A laparoscopic approach has been advocated for large defects (RM<3mm), in the presence of symptoms and desire to maintain fertility. **Conclusions.** The increasing prevalence of isthmocele, through its gynecological and obstetric complications, caused by the increasing number of caesarean sections (CS) deliveries performed worldwide, is alarming, therefore isthmocele should figure as a differential diagnosis in women with previous CS deliveries, especially in those with risk factors of multiple previous caesarean sections and retroflexed uterus.

Keywords: isthmocele, hysteroscopy, laparoscopy

Prolabation of a pedunculated endocavitary nodule as a result of hemostatic uterine curettage

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Introduction. Uterine leiomyomas are the most frequent tumors of the female genital tract. Giant uterine leiomyomas are very rare tumors and represent a major diagnostic and therapeutic challenge. **Materials and method.** This paper presents the clinical case of a 42-year-old patient hospitalized in our gynecology ward with a history of repeated metrorrhagia over the past six months, accompanied by low back pain, abdominal pressure, constipation and pollakiuria. The physical examination, laboratory investigations and ultrasound examination revealed the existence of a giant uterine tumor formation, located within the abdominal cavity. **Results.** As a peculiarity, this clinical case is made notable by the fact that, following the hemostatic uterine curettage performed due to massive bleeding on the CGE, the massive pedunculated submucosal endocavitary nodule migrated from the uterine cavity into the vagina, greatly dilating the cervix and exteriorizing through it. As a result, the giant abdominal tumor turned

into a pedunculated endovaginal tumor! **Conclusions.** In some cases, the submucosal fibroid may be attached to the uterus by a narrow stalk of tissue (peduncle) that allows the submucosal fibromatous nodule to slide into the vagina. This also happened in the case of our patient. The extremely small number of cases and the lack of reports in the literature also reflect the rarity of this pathology, while the complexity of the therapeutic conduct in the case of this tumor is directly proportional to its size. **Discussion.** The case presented is interesting due to the difficulties in clinical diagnosis, in terms of the origin and character of the tumor. One of the peculiarities of the case is represented by the tumor, how the pediculated uterine tumor behaved after the biopsic and hemostatic uterine curettage and its migration from the uterine cavity through the cervix to the vagina.

Keywords: pedunculated endocavitary nodule, prolapse, hemostatic uterine curettage

Frequency of urinary tract infection in pregnancy

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Introduction. Urinary tract infections are the most common medical complications in pregnant women, which occur due to anatomical and physiological changes during pregnancy, pregnancy hormones, reduced immunity in pregnancy and to bacterial contamination. Pregnancy is an important risk factor, with the frequency of pyelonephritis in pregnancy being found in 10% of urinary tract infections. **Materials and method.** The study was performed on a group of 150 pregnant women diagnosed with urinary tract infection during pregnancy and included their age, gestational age, medical history, the described symptoms and obstetric clinical examinations and paraclinical examinations (ultrasound, urine summary, urine culture, general blood tests, blood biochemical analysis). Of these, 105 pregnant women (70%) were diagnosed with cystitis, 30 pregnant women (20%) were diagnosed with urethritis and 15 pregnant women (10%) were diagnosed with pyelonephritis. A urinary tract infection in pregnancy is manifested in the bladder (cystitis), urethra (urethritis) and in the pelvis, renal calyx and renal parenchyma (pyelonephritis). Pregnancy pyelonephritis, in the absence of a specialized treatment, causes major complications. **Results and conclusions.** We note that the most common form

of urinary tract infection in pregnancy was cystitis – 70% (bacterial inflammation of the bladder), caused by bacteria in the anal area (*E. coli*) and by the fact that in women the urethra is shorter, which slight favors the contamination of bladder. Urethritis was found in 20% and pyelonephritis (infection of the pelvis, calyx and renal parenchyma) in 10% of cases. Pyelonephritis was due to low urinary tract infections that were not treated in a timely and appropriate manner, to increased progesterone levels in pregnancy with relaxation of muscle tone of the ureters, dilation and slowing of urine flow, compression of the ureter by the pregnant uterus with slowing of urine flow, reduction bladder tone, bladder reflux, increased acidity of urine in pregnancy, and to increased amount of glucose in the urine that promotes bacterial growth. **Discussion.** The repercussions of pyelonephritis on pregnancy are severe (imminent premature birth, early rupture of membranes, premature birth, IUGR, preeclampsia). Untreated urinary tract infection in pregnancy can lead to serious complications, therefore it is important to recognize the symptoms and to initiate the appropriate treatment.

Keywords: urinary tract infection, cystitis, urethritis, pyelonephritis, ureters, renal parenchyma

Incidence of vaginal candidiasis in pregnancy

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Introduction. Vaginal candidiasis is one of the most common genital infections during pregnancy. On average, three out of four pregnant women develop vaginal candidiasis. One of the most common types of fungus that live in and on the human body is called *Candida* (*Candida albicans*). **Materials and method.** The study was performed on a group of 200 pregnant women with pregnancies in the first, second and third trimesters; of these, 150 pregnant women (75%) were diagnosed with vaginal candidiasis. We took into account the medical history of pregnant women, the anamnesis, the general physical examination, the obstetrical clinical examination, and the paraclinical examinations (cytobacteriological examination, yeast culture on Sabourand medium, fungigram). Of the 150 pregnant women diagnosed with vaginal candidiasis, 30 pregnant women (20%) were in the first trimester of pregnancy, 30 pregnant women (20%) were in the second trimester of pregnancy, and 90 pregnant women (60%) were in the third trimester of pregnancy. *Candida albicans* is a fungus that is found in the normal flora of the vagina, and when it multiplies excessively and exceeds the protective flora, candidiasis occurs. Causes of vaginal candidiasis in pregnancy: changes of pH in pregnancy with reduced ability of the body's defenses, hormonal changes (increased estrogen levels) in pregnancy lead to increased glycogen – the main food for the development of fungus, highly processed foods

that have a high sugar content, low level of hygiene, consumption of antibiotics. **Results.** We note that three out of four pregnant women have vaginal candidiasis during pregnancy. *Candida albicans* normally exists in the mouth, intestines, skin and mucous membranes, usually in wet areas but without causing problems. When the conditions in the environment in which it lives change, this fungus multiplies uncontrollably, and the infection it causes is called candidiasis. **Discussion and conclusions.** Vaginal candidiasis can cause miscarriage, premature birth and chorioamnionitis with *Candida*. It is also one of the most common forms of fungal diseases reported in pregnant women that can cause systemic infections of newborns, especially in those who are underweight at birth and premature. Ideally, it is necessary to treat vaginal candidiasis before pregnancy, as well as early diagnosis during pregnancy with the administration of specific treatment – azol antifungals are recommended as therapy of choice during pregnancy and can be given as local creams or intravaginal suppositories (eggs) for seven days. Regarding the high incidence of vaginal candidiasis in pregnant women (3/4), it is very important for the future mother to remember that the safest treatment is the one prescribed by the doctor. This is the only way to get rid of recurrent candidiasis.

Keywords: *Candida albicans*, fungigram, cytobacteriological smear, estrogen, glycogen

Maternal and neonatal outcomes associated with delivery techniques for impacted fetal head at caesarean section – systematic review and meta-analysis

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Introduction. Late first-stage or second-stage caesarean section is commonly associated with fetal head impaction, leading to maternal and neonatal complications. This situation requires safe delivery techniques, but the optimal management remains controversial. The aim of this meta-synthesis was to compare maternal and neonatal outcomes associated with delivery techniques via caesarean section. **Methodology.** An electronic search of three databases, from inception to June 2021, was conducted. Cohort and randomized comparative studies on maternal and neonatal outcomes associated with techniques to deliver an impacted fetal head during caesarean section were included. The methodological quality of the primary studies was assessed. Review Manager 5.4 was used for statistical analyses. Nineteen articles, including 2345 women, were analyzed. **Results.** Three fetal extraction techniques were identified. Meta-analyses showed

that the “pull” technique carries lower risks as compared to the “push” technique, and that the Patwardhan technique is safer compared to the “push” or the “push and pull” technique. Nine out of 11 quality criteria of the included studies were fully met. The “push” and the “pull” techniques were investigated by most included studies. The “pull” technique showed lower risks of blood transfusion ($p=0.03$), extension of uterine incision ($p<0.00001$), infection ($p=0.003$) and pyrexia ($p<0.00001$) compared to the “push” method. **Conclusions.** In the absence of robust evidence to support the use of a specific technique, the choice of the obstetrician should be based on best available evidence. Our study suggests that the “pull”, as well as the Patwardhan technique represent safe options to deliver an impacted fetal head.

Keywords: caesarean section, impacted head, Patwardhan method, pull method, push method

Maternal anxiety scores correlated with childbirth perineal trauma – preliminary data of a cohort study

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Introduction. It is well known that severe obstetric lacerations are associated with anxiety disorders or even with postpartum depression among women. Very few studies investigated the levels of intrapartum anxiety caused by the eventuality of childbirth perineal trauma. This study aimed to evaluate maternal anxiety scores, intrapartum or during the first two hours postpartum, in different patient groups. **Methodology.** In March 2022, 44 consecutive primiparous women completed an anxiety visual scale, from 1 to 10, intrapartum or during the first two hours postpartum, reflecting their anxiety associated with obstetric lacerations. Six to 18 months postpartum, they will complete an International Consultation on Incontinence Questionnaire Vaginal Symptoms Module (ICIQ-VS), a standardized questionnaire to quantify the mid-term impact of perineal lacerations on vaginal symptoms, prolapse symptoms, sexual problems and quality of life. Moreover, correlations between the anxiety scores and ICIQ-VS scores will be sought. **Results.** GraphPad Prism 8 was used for statistical analysis. Mann-Whitney test was used for

comparisons among groups and Pearson coefficient was used for correlations. The women reported significantly higher anxiety scores correlated with childbirth perineal trauma during labor, compared to immediate postpartum ($p=0.0008$). Women receiving epidural analgesia reported higher anxiety scores compared to women without epidural, but the difference of scores did not reach the statistical significance ($p=0.142$). No statistically significant correlation was found between the age or Body Mass Index (BMI) of the included women and the reported anxiety scores ($p=0.142$ and $p=0.494$, respectively). **Conclusions.** Anxiety correlated with childbirth trauma is significantly higher during labor compared to the postpartum period in primiparous women. Patients with epidural analgesia did not report significantly different anxiety scores compared to patients without analgesia. In addition, demographic or anthropometric factors, such as age or BMI, did not significantly correlate with the anxiety scores in primiparous women.

Keywords: maternal anxiety, childbirth trauma, episiotomy, perineal lacerations, vaginal birth

Urinary infections during pregnancy

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Objectives. The aim of this study was to analyze the epidemiology and the potential for possible urologic surgery in pregnant women with associated urinary tract infections (UTI). **Materials and method.** We retrospectively analyzed the electronic records of all pregnant women admitted to the urology clinic at "Dr. C.I. Parhon" Clinical Hospital, Iaşi, with a diagnosis of UTI between 2017 and 2021. **Results.** During this period, 62 patients were selected, of whom 26 (41.9%) underwent surgery and 36 (58.9%) were treated with antibiotics only. Fifty-three cases (85.5%) had upper urinary tract infections (acute pyelonephritis or infected ureterohydronephrosis), and nine cases (14.4%) had lower urinary tract infections, but with physiological ureterohydronephrosis associated (UHN). The patients with cystitis but without physiological UHN were not hospitalized, being treated as outpatients, and were not included in the study. In 46 cases (74.2%), the UHN was on the right side, in 14 cases (22.6%) it was on the left side, and in two cases (3.2%) it was bilateral. In 25 cases (40.3%), a double J-insertion was performed, and in one case, a percutaneous nephrostomy was performed. In 20 cases (32.2%), the UTI was as-

sociated with a febrile syndrome. Most pregnant patients were admitted in the second trimester (37 cases; 59.6%), followed by the third trimester (18 cases; 29%) and the first trimester (17 cases; 27.4%). The most frequently identified germ was *E. coli* (80%), followed by *Klebsiella*, enterococci, staphylococci and *Serratia*. All patients developed well, with one exception who was transferred to the "Cuza Vodă" Clinical Hospital of Obstetrics and Gynecology, Iaşi, and presented with preterm labor. Six (23%) of the operated patients returned with reflux pyelonephritis, which responded well with antibiotic treatment. **Discussion and conclusions.** Urinary tract infections that occur during pregnancy can lead to high morbidity, especially preterm labor and fetal distress. Therefore, the immediate treatment with antibiotics, and even emergency urologic surgery, is required to avoid such complications. Nevertheless, pregnant patients wearing double J stents or nephrostomy catheters must be closely monitored to avoid reinfection with subsequent readmission to the urology clinic.

Keywords: urinary infections, pregnancy, preterm labor, fetal distress

Fetal neurological distress associated to maternal immune activation. Short- and long-term outcome

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Hypoxic ischemic, metabolic disorders, stress, socioeconomic factors, infections and inflammation, genetic/epigenetic conditions are potential causes of fetal distress, for neuromotor and neurodevelopmental disorders: cerebral palsy, neuromotor retardation, spastic tetraplegia, ASD, ADHD, Tourette syndrome, schizophrenia, usually depicted in childhood/adult life, and yet without complete knowledge for gestational prevention. The classical TORCH infections represent the catastrophic structural anomalies in the fetal brain, eye, ear, and human epidemiology and animal studies imposed a reconsideration of concepts regarding fetal brain jeopardize from early pregnancy, inflammation being a mandatory event – progesterone-dependent, in uterine and systemic immune modulation for pregnancy progression, and it is a midpregnancy brain window of vulnerability, with a recent step down in the gestational age of brain vulnerability. One reconsiders the pathophysiology under the concepts/terminology of fetal inflammatory response syndrome (FIRS), fetal brain damages – considered initially in preterm babies (preterm labor – a fetal “escape” episode), PROM – are actually also discussed in near term or late preterm births, under the new concept of perinatal telencephalic leukoencephalopathy. Maternal immune activation (MIA) in acute infections, systemic chronic inflammation, placental changes and fetal blood-brain barrier changes cooperate for offspring neurologic disorders and mental illness. The cytokine storm (maternal, placental, fetal) secreted by immune cells through TLRs – Toll-like receptors) with high blood levels of IL-6, IL-1 β , TNF- α and interferon γ is responsible for fetal brain damages without any fetal positivity for bacteria, viruses, fungi and protozoa, because of the primer role of MIA on fetal brain, a fact also recently proven in COVID-19. The complex fetal brain cellular network is affected, from physiological events of proliferation, migration, differentiation, myelination, programmed death, formation of synapses, in cerebral and hippocampus neurons and oligodendrocytes, activated of microglia and astroglia, enhancement of glutamatergic and GABAergic synaptogenesis, and placental serotonin system. The neuromotor and neurodevelopmental inflammatory induced disorders are suggested and depicted by the well-known nonspecific inflammatory criteria, in association to ultrasound, MRI, cardiotocography, umbilical cord blood IL-6 levels (>11 pg/ml) at birth, funisitis, and chorionic vasculitis (hallmarks fetal placental abnormalities associated to maternal chorioamnionitis), neurodevelopment monitoring/assessment after the first six postnatal months of life. Fetal brain injury represents a major interest for medical staff in effective human brain damage prevention on short and

long term. Hypoxic ischemic, metabolic disorders, stress, socioeconomic factors, infections and inflammation, genetic/epigenetic conditions are potential causes of fetal distress, for neuromotor and neurodevelopmental disorders (such as cerebral palsy, neuromotor retardation, spastic tetraplegia, ASD, ADHD, Tourette syndrome), usually depicted in childhood/adult life, and yet without a complete knowledge for gestational prevention. The classical TORCH infections represent the catastrophic structural anomalies in the fetal brain – anencephaly, ventriculomegaly, white matter severe neurodevelopmental delay, eye, ear, but human epidemiology and animal studies imposed a reconsideration of concepts regarding fetal brain jeopardize from early pregnancy, inflammation being a mandatory event in uterine and systemic immune modulation for pregnancy progression progesterone-dependent (NK, dendritic cells, special lymphocytes in decidua, cervix, placenta), being a midpregnancy brain window of vulnerability. One is reconsidering the pathophysiology under the concepts/terms of fetal inflammatory response syndrome (FIRS), fetal brain damages – considered initially in preterm babies (preterm labor – a fetal “escape” episode, PROM) – are actually discussed in near term or late preterm birth, under the new concept of perinatal telencephalic leukoencephalopathy. Maternal immune activation (MIA) in acute infections, systemic chronic inflammation, placental changes and fetal blood-brain barrier changes compete and/or cooperate for offspring neurologic disorders. The cytokine storm (maternal, placental, fetal), with high blood levels of IL-6, IL-1 β , TNF- α and interferon γ , is responsible for fetal brain damages without any fetal positivity for bacteria, viruses, fungi, protozoa, because MIA primer role on fetal brain in fetal programming immune system, fact proved also recently in SARS-CoV-2 infection. The physiological cellular fetal brain's events – proliferation, migration, differentiation, death – of the neurons and oligodendrocytes are early influenced, microglia and astroglia are activated, and the glutamatergic and GABAergic synaptogenesis, and placental serotonin system are enhanced. The neuromotor and neurodevelopmental disorders inflammatory induced are suggested and depicted by the well-known nonspecific inflammatory criteria, in association to ultrasound, MRI, cardiotocography, umbilical cord blood IL-6 levels at birth, the assessment of funisitis, chorionic vasculitis (fetal placental abnormalities associated to maternal chorioamnionitis), and neurodevelopment monitoring/assessment after the first six postnatal months of life.

Keywords: fetal neurovulnerability, fetal inflammatory response syndrome, maternal immune activation; infection/inflammation

Voluminous placental chorioangioma complicated with premature placental abruption

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Placental chorioangioma is the most common benign non-trophoblastic tumor of the placenta, occurring in approximately 1% of pregnancies. Most placental chorioangiomas are small and are not clinically important. However, those measuring more than 4-5 cm in diameter are rare and may be associated with maternal and fetal complications. We report the case of a voluminous chorioangioma diagnosed in a 30-week pregnancy asso-

ciated with premature placental abruption. Emergency caesarean section was performed with favorable maternal and neonatal outcome. Early diagnosis, close prenatal surveillance and appropriate intervention may prevent severe complications and perinatal mortality caused by chorioangioma.

Keywords: chorioangioma, placental abruption, placenta

Surgical challenges during pandemic period

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Introduction. COVID-19 pandemic is caused by SARS-CoV-2 and it has an important but often overlooked impact on surgical current activity. The reports about its implications in obstetrical and gynecological surgical side are accumulating. The purpose of our study was to reveal the surgical challenges during pandemic period. **Methodology.** We reviewed the main medical databases, such as PubMed, Medline and Web of Science, searching for publications about SARS-CoV-2 in surgery and we focused on reports about the challenges that medical staff had to endure during patients' care. **Results.** Our research revealed more than 4500 publications about SARS-CoV-2 and medical staff. At onset, there was a lack of information. The virus spread so fast, and the medical professional providers had different challenges. At the beginning, everybody was discussing

about the way of transmission among individuals. The deficit of equipment was a major reason of concern. The instructions of using correctly the PPE were contradictory. All the medical staff was stressed, and they must face more stressed patients with different pathologies. In time, the reasons of concern changed so that that surgical procedures can be performed in safety conditions for both surgeon and patient. The characteristic of each pandemic wave raised peculiar discussions. **Conclusions.** COVID-19 in gynecologic operating room represents a challenge because the physician has to perform usual surgical steps in special conditions. The literature experience and the personal one in COVID-19 hospital represent the subject of this report.

Keywords: SARS-CoV-2, surgery, COVID-19, complications

Group B Streptococcus and pregnancy

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Group B of streptococcal infection (*Streptococcus agalactiae*; GBS) in pregnancy remains an important cause of maternal and fetal morbidity and mortality. Ten percent to 30% of women are colonized during pregnancy. In the first days of life, fetal consequences of streptococcal B infection may lead to puerperal sepsis, meningitis, encephalitis or offspring pneumonia. Infant long-term consequences may determine neurological sequelae and mental disabilities, and very rare there are reported cases of late death of the child after some weeks of life. Therefore, without preventative measures, early-onset GBS infection may occur in 1% to 2% of neonates born to mothers with GBS colonization. The maternal consequences of streptococcal B infection are represented by endometritis and sepsis. This pres-

entation is an update about streptococcal B infection in pregnancy. Universal screening and antibioprophyllaxis during labor are safe and effective. Antibiotherapy for vaginal colonization is not recommended. Also, systematic cultures in neonates in the third trimester of pregnancy do not detect antenatally all GBS carriers. Routine intrapartum prophylaxis for carriers of SGB does not appear to affect the long-term complications. Better laboratory tests for identifying serotypes, genotypes and phenotypes must be available, significantly to differentiate between streptococcal high- and low-risk infections regarding maternofetal consequences. Immunization remains a promising way to eradicate this infection.

Keywords: GBS, pregnancy

Vaccination during pregnancy

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Vaccination during pregnancy is demonstrated to have a dual beneficial effect on the mother and the offspring by preventing infections. Pregnant women are at high risk of infectious diseases, some of these being vaccine-preventable diseases. In Europe, influenza, tetanus, diphtheria and pertussis are preventable infectious diseases for which vaccinations are routinely recommended during pregnancy. Due to the reluctance for vaccine administration during pregnancy and to lack of trials approach, this topic aims to present the current knowledge on vaccinations in pregnant women as a useful information source for patients and healthcare workers involved in pregnancy monitoring. In addition, good-quality scientific information must be used to prevent myths and misconceptions, such as those stating that all prophylactic or therapeutic pharmaceutical products, including vaccines, must be avoided in pregnancy. Moreover, the anti-rubella vaccination in the postpartum period is highly recommended to nonimmunized women. The safety and effectiveness of authorized vaccines in pregnancy are proven, even though the pregnant woman is considered a “vulnerable” person, and most clinical trials specifically exclude these individuals. We present the current knowledge about routine and contraindicated vaccines during pregnancy. Also, we argue about vaccines that may be used only in exceptional extenuating circumstances, such as preventing cytomegalovirus or *Streptococcus B* infections.

Keywords: vaccination, pregnancy, influenza, diphtheria, pertussis, COVID-19

Medullary aplasia in pregnancy – obstetrical and maternal risk. Case presentation and literature review

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Introduction. The first case of medullary aplasia was described in literature in 1888 by Paul Ehrlich in a pregnant woman who died of postpartum hemorrhage. The term *medullary aplasia* is similar to that of *aplastic anemia*. Aplastic anemia is a syndrome of medullar damage characterized by pancytopenia (leukopenia, thrombocytopenia, erythropenia) and medullary hypoplasia; it is a rare and serious condition which has an increased risk of maternal and fetal complications. **Materials and method.** We present the case of a pregnant 28-year-old patient who presented at the emergency room for systemic painful uterine contractions, spontaneously ruptured membranes with clear liquid exteriorization on the external genitalia and skin pallor. From the laboratory analyzes, we mention normochromic normocytic anemia (Hb=9.7 g/dL), leukopenia ($2.19 \times 10^3/\mu\text{L}$), erythropenia ($3.12 \times 10^6/\mu\text{L}$) and neutropenia ($1.2 \times 10^3/\mu\text{L}$). At the local clinical examination, there is a clear cervix, with 2 cm dilatation, cranial presentation, mobile and spontaneously ruptured membranes. Ultrasound biometry showed a pregnancy of 38 weeks and 6 days,

single live fetus, cranial presentation, grade 3 posterior placenta, a small quantity of amniotic fluid, 146 BPM fetal heartbeats, and an estimated weight of 3400 grams. The diagnosis was: IG IP pregnancy, a 39-week single live fetus, with cranial presentation, spontaneous ruptured membranes, triggered birth, medullary aplasia, secondary anemia and negative birth test. Caesarean section was performed to extract one single live fetus, male, weighing 3450 grams, with an Apgar score of 9. **Results.** The evolution was favorable for both the mother and the fetus. Cyclosporine A has been shown to be effective during pregnancy, but at the patient’s request, the administration of CyA treatment was discontinued during breastfeeding, as it excreted in breast milk. **Conclusions.** Pregnancy associated with medullary aplasia increases the risk of maternal and fetal complications and, thus, it is necessary to form a multidisciplinary team to monitor the pregnancy in order to obtain the optimal results.

Keywords: aplasia, pregnancy, cyclosporine, leukopenia, neutropenia

Maternal group B streptococcal infection/colonization and neonatal consequences

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Streptococcus agalactiae (GBS) is a commensal germ of the genitourinary and gastrointestinal tracts. The colonization rate in pregnant women varies between 10% and 35% and, during pregnancy, colonization can be constant or intermittent. GBS colonization is associated with low maternal age, chronic hypertension, preexisting diabetes mellitus and smoking. In addition to maternal infection, GBS can cause severe infections in the newborn, either early in birth, with vertical transmission, or later, in case of horizontal transmission. Vertical transmission occurs when no intrapartum antibiotic prophylaxis is performed, and the lower the gestational age, the higher the risk of infection. Specialized international academic forums recommend both universal screening through vaginal/rectal cultures at 36-37 gestational weeks, as well as adequate implementation of intrapartum antibiotic prophylaxis, at least two (preferably four)

hours before any obstetric intervention. Intrapartum antibiotic prophylaxis should preferably use penicillin G, due to its narrow spectrum and low probability of inducing resistance to other vaginal microorganisms. If there is a risk of allergic reactions, ampicillin, first-generation cephalosporins, clindamycin or vancomycin are indicated in this order and depending on the sensitivity of the GBS on the antibiogram. In the newborn, the treatment of GBS infection is performed using penicillin G or ampicillin, depending on the gestational age, postnatal age and the type of involvement (pulmonary/systemic or meningeal). In conclusion, systematic screening and intrapartum prophylaxis with antibiotics may lead to a decrease in morbidity and mortality due to neonatal GBS infection.

Keywords: group B *Streptococcus*, screening, intrapartum antibiotic prophylaxis

Increasing patients' confidence in medical-pharmaceutical services

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Introduction/objective. Patient's satisfaction is an important indicator for both the doctor and the pharmacist. The literature shows that there is a direct proportional relationship between the degree of trust in health professionals and the patients' adherence to treatment. The medicines are prescribed by the doctor, made and delivered by the pharmacist, together with the necessary recommendations and advice. The patient's perception and the degree of trust in specialists influence the adherence to treatment of patients and affect the medical outcomes. In this context, this study aimed to investigate patients' perceptions on compounded medicines (CM) and how this perception influences the degree of trust in medical-pharmaceutical services. **Methodology.** The survey was conducted in community pharmacies in Iași, Romania (n=10), by distributing a questionnaire to patients (n=1000), after pharmaceutical act achievement by the pharmacist. The questionnaire contained items that marked the perception of the difference between CM

and industrial medicines (IM) and the degree of trust in medical-pharmaceutical services. **Results.** A response rate of 69.9% was recorded. 71.5% of respondents know the medicines prepared in the pharmacy under the name of CM. 68.1% used CM at least once. 64.5% would like to continue using an CM. The correlation ($r=0.682$ and $p=0$ [<0.0006]) indicate, in patients who used CM, a degree of confidence of 82% in medical-pharmaceutical services. **Discussion and conclusions.** Patient's satisfaction has become an increasingly researched topic, in an attempt to provide the most appropriate solutions for the management of medical institutions, in order to maximize the obtained results, from a medical and managerial point of view, including the image of the institution on the market. Despite the fact that CM are less used compared to IM, this study shows that the degree of trust of patients in specialists who recommend and prepare CM is 82%.

Keywords: patient, questionnaires, medical-pharmaceutical services

Treatment of nosocomial infections with *Candida* species: clotrimazole versus miconazole

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Introduction/objective. Nosocomial infections are a real public health problem that can complicate long-term health systems. Patients are exposed during hospitalization to a variety of pathogens of bacterial, viral or fungal nature, and candidiasis is increasingly reported in patients with prolonged hospitalization in intensive care clinics. This study aims to evaluate the influence of excipients from pharmaceutical formulations with clotrimazole (50 µg) and miconazole nitrate (50 µg) on antimicrobial activity on various strains of *Candida*, by establishing minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (CMBs).

Methodology. Three types of *Candida* strains were used: *Candida albicans* ATCC 10231, *Candida sake* and *Candida glabrata* ATCC MYA 2950 grown on a Sabouraud (Fluka) agar medium and the antimicrobial activity of miconazole (50 µg) and clotrimazole (50 µg) pharmaceutical formulations were compared to control – nystatin (100

µg). After 24 hours of incubation, the MIC value was recorded as the lowest concentration of the sample in which the visible growth of microorganisms is absent.

Results. The investigated pharmaceutical formulations of miconazole nitrate and clotrimazole showed superior activity on the tested strains of *C. albicans*, *C. glabrata* and *C. sake* compared to the control nystatin. The miconazole nitrate dosage formulations were found to have a larger inhibition area diameter on *Candida albicans* compared to those containing clotrimazole. **Discussion and conclusions.** The tested miconazole nitrate pharmaceutical formulations can be successfully used in nosocomial infections with *Candida albicans*, acting by inhibiting the synthesis and incorporation of ergosterol into the fungal cell membrane following the blockade of sterol-14 α -demethylase, a cytochrome P450-dependent enzyme important in ergosterol biosynthesis.

Keywords: miconazole nitrate, clotrimazole, nystatin

Reproduction immunology

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Introduction. Human reproduction is a vast field, in continuous research. Reproductive immunology represents the medical area that deals with the interactions between the immune response and the reproductive system and the adaptation of the mother’s body to pregnancy and abortive disease regarding the response to embryonic “stimulus” may influence the new treatments and the understanding of pregnancy in the immune context. Among the problems that can cause infertility, there are the immune dysfunctions of the human reproductive system. **Methodology.** This

presentation is a literature review with interest in information on reproductive immunology. **Discussion.** Human reproduction has many influencing factors, but adaptive immunological mechanisms are an area to consider given the pathology associated with reproduction. **Conclusions.** Normal reproductive function is given by the interaction, not the competition of the immune and reproductive systems from the formation of gametes to fertilization, implantation and the balance of the mother-fetus interface.

Keywords: immunology, reproduction, fertility

Female and male infertility in the time of pandemic

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Introduction. The increased social and economic burden caused by the novel COVID-19 outbreak is gradually becoming a worrisome issue for the health sector. The novel coronavirus invades the target cell by binding to ACE2, which is widely expressed in the ovaries, uterus, vagina and placenta. Significantly, the SARS-CoV-2 is said to interrupt female fertility through regulating ACE2. Thus, it is essential to investigate if SARS-CoV-2 infection hampers female fertility, given that there is no systematic and comprehensive evidence on the association of COVID-19 with fertility. **Materials and method.** We performed a web research regarding male and female fertility and COVID-19. The eligibility criteria included: population aged 13–49 years old; exposure (infection with SARS-CoV-2); comparison (population without SARS-

CoV-2 infections or latent SARS-CoV-2 infections); and outcome (female fertility, such as ovarian reserve function, uterine receptivity, oviducts status and menstruation status, male fertility and parameters). **Results.** Some studies showed that COVID-19 vaccines don't impair fertility in men or women, but SARS-CoV-2 infection could potentially affect a man's fertility for up to 60 days; for example, being 18% less likely to conceive during the next cycle of their female partner, compared with men who had not tested positive. **Conclusions.** Further data need to be acquired to synthesize the new effects on the population. Any infection – particularly an infection that involves fever – can affect sperm production and can affect ovulation, factors that apply in COVID-19.

Keywords: COVID-19, fertility

Contraceptive methods in HIV pathology

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Introduction. Meeting the contraceptive needs of women living with HIV (WLHIV) has primary health benefits for them, in addition to being a key element to prevent mother-to-child HIV transmission. This analysis will estimate the current number of infant HIV infections prevented by contraception. **Methodology.** We performed a literature search of PubMed to identify reports of drug interactions between hormonal contraceptives (HCs) and antiretroviral drugs (ARVs). We also reviewed the guideline of contraceptive hormone preparations and antiretrovirals for additional data and recommendations. **Results.** Several studies of combined oral contraceptive pills (COCs) identified decreased serum estrogen and progesterin levels when co-administered

with certain ARVs. The contraceptive efficacy of injectable depot medroxyprogesterone acetate (DMPA) and the levonorgestrel intrauterine system (LNG-IUS) were largely unaffected by ARVs, while data on the contraceptive patch, ring and implant were not significant information to mention. **Conclusions.** Contraception continues to play an integral role in global HIV prevention efforts in the era of increasing HIV treatment coverage, especially in poor-income countries. Broad contraceptive availability, increased contraceptive voluntarism and method mix are key components to preventing unintended births and ending new infant HIV infections worldwide.

Keywords: hormonal contraceptives (HCs), antiretroviral drugs (ARVs), HIV

Impact of caplacizumab therapy on thrombotic thrombocytopenic purpura in pregnancy: case report and literature review

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Thrombotic thrombocytopenic purpura (PTT) is a rare disease, being a hematological emergency, which requires the initiation of plasmapheresis and immunosuppressive treatment as soon as possible. **The aim** of this paper is to present a clinical case of PTT that is associated with pregnancy and in which caplacizumab has been administered. **Clinical case.** We present the case of a patient who presented the first episode of PTT at the age of 27 years old in the context of a stopped pregnancy evolving at 24 weeks. The second episode of PTT appeared at the age of 32 years old, in the context of a second pregnancy with the onset of thrombocytopenia at the gestational age of 37 weeks. Coadministration of caplacizumab with plasmapheresis resulted in the rapid normalization of platelet counts and in a significant shortening of the hospitalization. The therapeutic response is maintained six weeks after the last dose of caplacizumab. **Discussion.** The diagnosis of thrombotic thrombocytopenic purpura is based on the presence of thrombocytopenia and microangiopathic hemolytic anemia, being confirmed by

decreased activity of the ADAMTS-13 enzyme. The differential diagnosis in our case required the exclusion of other pathological conditions that develop with anemia and thrombocytopenia. It can be associated with various physiological and pathological conditions, pregnancy being one of these conditions. PTT treatment consists of plasmapheresis and immunosuppressive therapy. Despite early treatment, mortality remains high, with a risk of disease recurrence. Caplacizumab is a nanoantibody that acts targeted on von Willebrand factor ultra-large multimers, with an impact on the evolution of PTT, a fact confirmed by the clinical case presented. **Conclusions.** Thrombotic thrombocytopenic purpura remains a diagnostic challenge, pregnancy being one of the conditions with which it can be associated. The administration of caplacizumab in the centers that run the PTT program is the first-line treatment, with a significant impact on the evolution and prevention of disease recurrence.

Keywords: pregnancy, thrombotic thrombocytopenic purpura, caplacizumab

Hemophilia in women – from theory to clinical reality

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Hemophilia is an inherited or acquired coagulopathy that can cause spontaneous or induced bleeding. Among the hemorrhagic manifestations, menorrhagia is common in women with coagulation disorders. These coagulopathies are frequently underdiagnosed in women. The aim of this paper is to update data from the literature on the diagnosis, clinical manifestations and treatment of hemophilia in women. **Materials and method.** Revision of data from the literature, as well as from the national protocol for the treatment of hemophilia and von Willebrand’s disease. **Results and discussion.** Congenital hemophilia in women exists, although this coagulopathy is frequently described in men, women being described as carriers. Over 50% of women with hemophilia A may experience bleeding, and menorrhagia is a common cause. The dosage of factor VIII

activity shows that they have a mild form of hemophilia. Moderate or severe forms of hemophilia, although rare, may occur in women in the context of an X monosomy, inactivation of an X chromosome, or impairment of both X chromosomes. Acquired hemophilia occurring due to the development of coagulation factor VIII or IX inhibitors occurs equally in men and women. In women it is often cited in the context of pregnancy or in the postpartum period. One of the common manifestations found in women with hemophilia is menorrhagia, which is why it becomes important to differentiate between a normal and a pathological menstruation. **Conclusions.** Hemophilia in women exists, the hemorrhagic manifestations represented by menorrhagia being frequently overlooked.

Keywords: hemophilia, menorrhagia, factor VIII

Pregnancy prognosis after conization for cervical carcinoma *in situ* – cases and overview of data from literature

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Unfortunately, young women are diagnosed with severe cervical dysplasia or even cervical carcinoma *in situ* (CIS) in Romania. Consequently, we can expect a higher percentage of pregnancies in patients with a history of conization than before. **Materials and method.** We present three cases with cervical CIS which were treated in a conservative manner by conization at 27, 34 and 30 years old, respectively. We also reviewed data from the literature. **Results.** The patients were nulliparous. The first woman obtained a subsequent pregnancy after one year and another one at five years after the procedure. She delivered both children by caesarean section (CS) at term. The second patient was with subfertility and performed an IVF (*in vitro* fertilization) 44 months after conization without success, but she obtained a pregnancy one month later, spontaneously. Her pregnancy has now 18 weeks. The prophylactic cerclage of the cervix was not necessary for these women. The third patient had also infertility and she is 35 years old now. Many

risk factors of preterm delivery (PTD) in patients with prior conization have been suggested, including the type of conization, second-trimester cervical length, specimen volume rather than "depth" (or "height"), and the interval between procedure and conception. As for the need for prophylactic cerclage, controversy still exists. It seems that cerclage is an independent risk factor for early PTD in patients who had a conization, compared with no cerclage. It was reported a significant increase in pathogenic flora in the vagina and cervix after cerclage. Antibiotics and tocolytics use, hospital admission, PTD, preterm rupture of membrane and CS rates were increased for these women with prophylactic cerclage. **Conclusions.** Cerclage procedures in women who underwent conization should not be performed routinely, unless supported by ultrasound evidence. An excisional treatment may affect subsequent fertility.

Keywords: conization, cervical carcinoma *in situ*, pregnancy, cerclage

Fetal cardiac evaluation in HIV-positive pregnant women under HAART

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Introduction. Human immunodeficiency virus is a virus that causes AIDS (acquired immunodeficiency syndrome), a disease that has a major socioeconomic impact. **Materials and method.** In our study, we tried to assess both fetal heart structure and function in HIV-positive pregnant women under antiretroviral therapy (HAART – highly active antiretroviral therapy). It was a prospective study that took place between January 2018 and December 2019. The hearts of 14 fetuses from HIV-positive pregnant women on antiretroviral therapy were assessed. **Results.** We found some statistically significant sex-related cardiac changes in HIV-exposed uninfected fetuses. We detected a narrowing of the aorta in female fetuses and also smaller left ventricular trans-

verse diameter in male fetuses. The myocardial performance index remained unaltered. **Discussion.** Because the majority of the patients included in this study had undetected viral loads, the effects on cardiac structure and function seems to be due to antiretroviral therapy. The effects of antiretroviral therapy on fetal heart seem to be sex-related. **Conclusions.** A more complete image about the risks and benefits of antiretroviral treatment, and also adopting management strategies to improve fetal outcomes, may also ensure better compliance of mothers to this vital treatment, that succeeded in turning a high mortality disease in a chronic one, with rates of survival similar to those of unaffected people.

Keywords: HIV, AIDS, HAART, pregnancy

Unusual types of leiomyoma – rare complication of minimally invasive surgery with morcellation

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Introduction. Uterine leiomyomatosis is the most frequent benign condition of female reproductive age, with a largely underestimated prevalence due to focusing only on symptomatic patients. There are some extremely rare and diagnostic challenging extrauterine localization of leiomyomas and also, unusual growth patterns. The etiopathogenesis remains incompletely understood, being probably complex, but it seems to be highly related to prior surgeries performed for uterine leiomyomas, especially those involving morcellation.

Materials and method. We studied English literature for unusual growth patterns of leiomyomas, selecting reports of these particular types of tumors from the period 1952-2018. **Results.** A total of 274 patients with parasitic leiomyoma were identified, 106 of them with a history of morcellation. We identified 161 cases reported of leiomyomatosis peritoneal dissemination.

Of the 161 women, 16 were menopausal and 145 were non-menopausal. A mechanical morcellation had been carried out in 22 cases. **Discussion.** The pathogenesis of these two entities is multifactorial, but laparoscopic morcellation is believed to play a substantial role. These conditions are not only associated with this type of surgery. There are cases in literature associated with open surgery for myomas, and also cases with no prior history of myoma. The main risk for developing this affection remains the simple presence of a uterine leiomyoma. **Conclusions.** Recently, the number of cases has increased due to the widespread of laparoscopic surgery and to power morcellation. A solution that might offer a better alternative is to perform the morcellation in a containment bag.

Keywords: laparoscopy, leiomyoma, extrauterine localization of myomas

First-trimester screening for aneuploidy in HIV-positive pregnant women under HAART

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Introduction. Human immunodeficiency virus (HIV), that ultimately determines the development of AIDS, evolved in time in a pandemic disease. **Objectives.** Our study evaluated first-trimester markers for aneuploidy in HIV-positive pregnant women under HAART (highly active antiretroviral therapy). **Materials and method.** This was a prospective study that took place between January 2018 and December 2019 in the “Cuza Vodă” Clinical Hospital of Obstetrics and Gynecology, Iași, Romania. We analyzed first-trimester PAPP-A (pregnancy-associated plasma protein A) and β HCG (β human chorionic gonadotropin) levels in 25 HIV-

positive pregnant women under HAART and compared them with the values of these markers in 31 seronegative pregnant women. Results. Both β HCG and PAPP-A were lower in HIV-positive women under HAART. **Discussion.** These alterations of first-trimester markers for aneuploidy might lead to an overestimation of the risk for Down syndrome. **Conclusions.** Obstetricians need to know the alterations of first-trimester markers for aneuploidy, so that they can correctly advise these women accordingly.

Keywords: HIV, AIDS, HAART, beta HCG, PAPP-A, aneuploidy

The accuracy of placental protein 13 (PP-13) for the first-trimester screening of preeclampsia

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Introduction/aim. Placental protein-13 (PP-13) is a member of the galectin group, involved in placental implantation, maternal artery remodeling and placental inflammatory processes. Its levels are lower in the first trimester for pregnancies later affected by ischemic placental disease and slowly increase during the second and third trimesters of pregnancy. The aim of the present meta-analysis is to assess the predictive performance of PP-13 in first-trimester preeclampsia (PE) screening. **Methodology.** PubMed, Web of Science, Scopus, Embase, BIOSIS and Cochrane databases were used to find relevant studies. All prospective and retrospective observational studies that evaluated the accuracy of PP-13 in predicting preeclampsia were assessed. The investigation revealed that the quantitative synthesis was based on 14 studies. **Results.** In studies that analyzed women with PE without subclassifying the population into early-onset PE (EO-PE) and late-onset PE (LO-PE), the pooled sensitivity of PP-13 was 0.53 (95% CI; 0.08-0.99; I² 0.0%) and the

pooled specificity of PP-13 was 0.83 (95% CI; 0.38-1.29; I² 0.0%). The summary receiver operating characteristic curve (SROC) was 0.88 (95% CI; 0.80-0.94). In the group of studies that categorized EO-PE separately, the pooled sensitivity of PP-13 was 0.51 (95% CI; -0.04-1.05; I² 0.0%), with a specificity of 0.88 (95% CI; 0.33-1.42; I² 0.0%). The area under the SROC was 0.69 (95% CI; 0.54-0.81). In the LO-PE group, the pooled sensitivity of PP-13 was 0.58 (95% CI; -0.17-1.33, I² 0.0%), with a specificity of 0.85 (95% CI, 0.10-1.60, I² 0.0%). The area under the SROC was 0.77 (95% CI, 0.63-0.87). **Discussion and conclusions.** The sensitivity analysis revealed a higher accuracy of PP-13 for the LO-PE screening compared to EO-PE. The incorporation of this biomarker in the first-trimester screening algorithms that combine maternal characteristics, sonographic parameters and serum biomarkers could be a viable option.

Keywords: placental protein-13 (PP-13), preeclampsia, first-trimester screening

Group B Streptococcus infection in pregnancy

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Introduction/objective. Group B *Streptococcus* (GBS) is normally found in the body. This is one of the important factors that should be investigated during pregnancy. In women, group B *Streptococcus* is most often found in the vagina and rectum, which is why there is a risk of transmission from a pregnant woman to the fetus during labor, the chances of which decrease when the mother receives treatment. **Methodology.** For this paper, we consulted studies in the literature and selected the essential information on the complications of this infection. **Results.** Pregnant women are tested for GBS

as part of routine prenatal care between 36 and 38 weeks of pregnancy. If the results show that GBS is present, most women will receive intravenous antibiotics once the labor has begun. This is done to help protect the fetus from being infected. The best time for treatment is during labor. Penicillin is the most commonly used antibiotic to prevent early-onset disease in newborns. **Discussion and conclusions.** Pregnant women should be tested for GBS, and if the test is positive, the baby can be monitored for GBS after birth.

Keywords: *Streptococcus* B, infection, penicillin

ZIKV infection in pregnancy

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Introduction/objective. Zika virus (ZIKV) is a dangerous infectious agent, due to its potential to cause severe teratogenic results, especially an abnormal brain development – microcephaly. It is also well known that the most common geographical areas for the transmission of this disease are South and Central America, South Asia, the Pacific region and, in particular, the United Kingdom, which is contracted by mosquito bites. **Methodology.** For this paper, we consulted studies in the literature and selected the essential information on the complications of this infection. Results. Pregnant women are advised to avoid traveling to these areas or contraception for three months after returning from one of these regions. Like

other agents, ZIKV can be transmitted vertically through the placenta during pregnancy, with potentially harmful consequences for the fetus. The easy clinical presentation made it difficult to establish a case definition for ZIKV infection in pregnant women. Zika virus infections during pregnancy are mainly identified using nucleic acid amplification and serological tests. **Discussion and conclusions.** While highly sensitive and specific laboratory diagnostic tests will improve the identification of maternal ZIKV infection before severe fetal abnormalities occur, there are currently no antivirals available to prevent the vertical transmission of Zika virus to humans.

Keywords: ZIKV, infection, microcephaly



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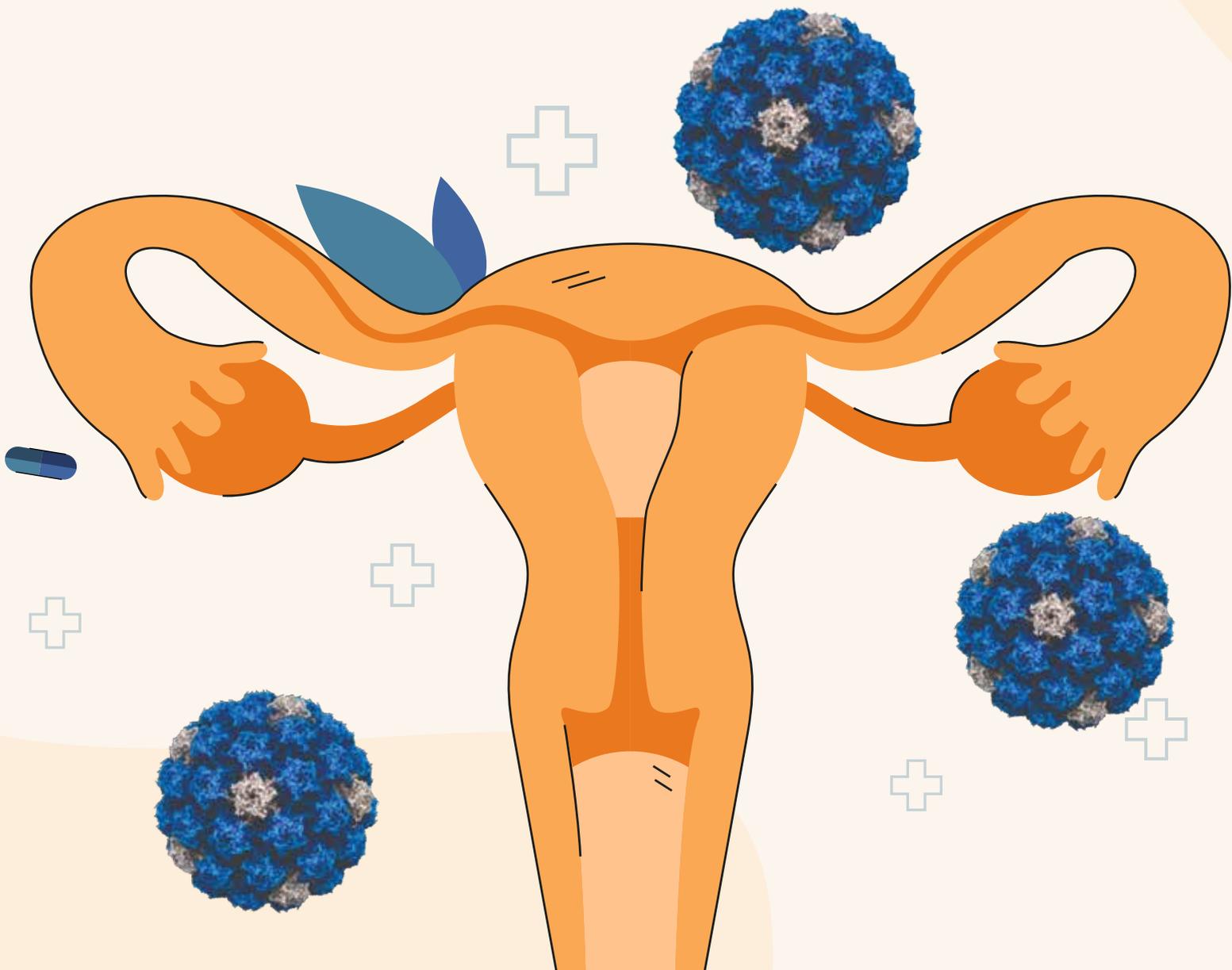


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The preimplantation genetic testing for monogenetic disease (PGT-M) in von Hippel-Lindau syndrome associated with non-obstructive azoospermia

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Introduction. Preimplantation genetic testing for monogenetic disease (PGM) is a highly advanced medical approach in monogenic disorders in which the disease locus is unequivocally described. For example, Von Hippel-Lindau syndrome (VHL) is a rare autosomal dominantly cancer syndrome characterized by multiple vascular tumors development. The costly diagnosis and surgical treatment of this disease cause severe problems to the patients and their families. **Materials and method.** We present a couple's case in which the husband was diagnosed with VHL and nonobstructive azoospermia. The couple decided on assisted reproductive technology treatment (ART). Before starting the IVF (*in vitro* fertilization cycle), extensive reproductive and genetic counseling is provided to the prospective parents. Particularly in monogenic diseases, there is necessary a preclinic genetic work-up. **Results.** We performed IVF stimulation with antagonist mixed protocol, obtaining ten mature oocytes.

The sperm was surgically extracted through TESE (testicular sperm extraction). We got four embryos after ICSI (intracytoplasmic sperm injection), only one being a good quality blastocyst that could be biopsied. In this case, we perform both PGT-A and PGT-M analysis using an NGS (following genetic sequence) platform. The PGT-A result was expected, but PGT-M showed the presence of VHL syndrome, so we decided not to transfer the embryo. The couple is determined to have another procedure to obtain a healthy baby. **Conclusions.** The patients became more aware of the genetically transmitted diseases and the number of conditions with identified genetic causes continues to expand. All in one solution, meaning PGT-A associated with PGT-M, is the solution in such cases. At this moment, the studies don't remark a difference between natural babies and those conceived after ICSI and PGT-M.

Keywords: genetic testing, Von Hippel-Lindau syndrome, azoospermia

Ovarian carcinoma associated endometriosis – case reports

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Introduction. In the general population, the risk of ovarian cancer is 1.31%, while in patients with ovarian endometriosis, the risk of ovarian cancer rises to 1.8%. Endometriosis shares common pathological mechanisms with cancer: abnormal tissue multiplication, the presence of local and distant implants, resistance to apoptosis and invasion of other tissues. Regarding the histopathological subtypes, it is known that the endometrioid and the clear cell carcinoma prevail among ovarian cancers. This association with malignancy of a condition otherwise considered benign should be acknowledged in order to properly advise the patients with endometriosis. Studies have shown that tumor volume is linked to the malignancy association risk and the advanced age (over 50 years old) is a significant risk factor also. **Materials and method.** We present two cases of ovarian endometriosis associated with ovarian cancer that were admitted to the Obstetrics and Gynecology Department of the Bucharest University

Emergency Hospital in 2020 and 2022. The ages of our patients were 33, respectively 32 years old, with large tumors, first with a long history of chronic pain, and the second with acute complains, and both underwent surgery, the definitive histopathological report revealing the association of ovarian carcinoma. We present the cases' evolution starting from the initial symptoms, imaging studies and laboratory results, treatment planning, surgical approach and findings, surgical and oncological follow-up. Furthermore, for endometriosis associated ovarian cancer, we discuss several favorable prognostic factors, such as early stage at diagnosis, low-grade disease, endometrioid or clear cell histology, resulting in low invasiveness and slow growth. **Conclusions.** We recommend that, despite being low, the malignancy risk in cases of ovarian endometriosis should be considered during patient counselling.

Keywords: ovarian endometriosis, ovarian cancer, endometrioid

Management of premature ovarian insufficiency in patients with endometriosis

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Endometriosis is a relatively common pathology that frequently affects the general population, found in approximately 10% of women of reproductive age. Although most often multiple endometriosis foci are found, the ovaries are the most prevalent location, approximately 20-40% of the patients suffering from ovarian endometriosis cysts. Women of reproductive age are at risk of developing premature ovarian failure, determined by the affliction itself, which causes chronic inflammation of the ovarian cortex and increased oxidative stress and folliculogenesis disarray ("burnout theory"), as well as the repetitive, most often bilateral, therapeutic surgical interventions. These repeated and chronic aggressions lead to a denaturation of the ovarian cortex, a lower AFC (antral follicular count) and, subsequently, to a lower AMH (anti-müllerian hormone). Premature menopause is characterized by the cease of ovarian function before the age of 40, impacting the

cardiovascular, nervous and osseous systems. In women of young reproductive age with endometriosis who have not yet completed family planning, the potential risk for low ovarian reserve, POI (premature ovarian insufficiency) and future infertility must be carefully assessed. These patients frequently need assisted reproduction techniques in order to obtain pregnancy. *In vitro* fertilization (IVF) has better outcomes if the patient had the opportunity to store oocytes (egg cells) or ovarian tissue before surgery. In patients with early menopause, although the reproductive function cannot be recovered, hormone replacement therapy (HRT) is recommended in order to lower the systemic affections. In patients suffering from endometriosis, this therapy may be considered, but we need to take into consideration the risk of disease reactivation.

Keywords: endometriosis, premature ovarian insufficiency, infertility, hormone replacement therapy

Improving IVF outcome by using DHEA in a patient with two previous failed IVF attempts

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Introduction. Adding DHEA supplement for 6-8 weeks before IVF cycle improves the outcome. **Case report.** We present the case of a 40-year-old patient, diagnosed with secondary infertility for three years, with one childbirth at the age of 14. The patient had three IVF cycles, using an antagonist protocol with 300 IU of gonadotropins. In the first IVF cycle, the number of oocytes was poor, the patient had a day 3 embryo transfer, the pregnancy occurred, but it was stopped for a malformed embryo. 25 mg DHEA daily was used after the first IVF cycle. In the second IVF cycle, we

observed a better number of oocytes, without reaching the blastocyst stage embryo transfer. In the third IVF cycle, still using DHEA supplement, the patient had a day 3 embryo transfer, resulting in pregnancy with term delivery of a healthy girl. **Conclusions.** Considering the patient's age correlated with the poor ovarian reserve, the supplementation with DHEA proved its benefit in the number of oocytes and the quality of the embryos.

Keywords: DHEA (dehydroepiandrosterone), IVF (*in vitro* fertilization), oocytes, pregnancy

Endometriosis and endometriosis-related ovarian cancer

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It is well known that ovarian cancer is one of the most severe forms of cancer in women, with high mortality and morbidity. Ovarian cancers can be classified in type I and II. There are almost 100 years from the first discussion regarding the relationship between endometriosis and ovarian cancer, stated by Sampson in 1927. Current studies have observed that the prevalence of ovarian cancer varies between 0.7% and 17% in women with endometriosis. The pathogenetic process of endo-

metriosis as cancer precursor was understood with the help of molecular medicine and genetics. The aim of this presentation is to summarize the current knowledge on endometriosis-related ovarian cancers. Understanding the pathologies can help to better select the patients with endometriosis who need further screening for ovarian cancer.

Keywords: endometriosis-related ovarian cancer, pathogenesis, screening

New biomarkers in endometriosis – a revision of data from literature

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Introduction. Endometriosis is a chronic neuroinflammatory disorder associated with important chronic pelvic pain, affecting approximately 6-10% of women of reproductive age. The diagnosis of endometriosis is often delayed because symptoms such as pelvic pain and/or infertility are associated with other disorders. The identification of biomarkers and endometriosis-specific noninvasive diagnostic tests represents a goal of the entire scientific community. The present paper aims to harmonize the results of these studies in the research for new promising perspectives regarding early diagnosis. **Materials and method.** The analysis of articles published in literature for evaluating new biomarkers that play a part in early identification of patients with endometriosis, but also in evaluating the response to the treatment. **Results.** The majority of the studies focused on a panel of biomarkers, rather than focusing on a single biomarker, and they couldn't identify at least one bio-

molecule or biomarker panel with enough specificity and sensibility in endometriosis. Recently, promising data regarding the utilization of blood micro-RNA as biomarker have appeared, although this domain has been previously underestimated by poor reproducibility between studies. The differential expression of miR-145 has been reported in the highest number of studies (six articles). Using saliva and vaginal fluid samples to identify miRNA could be a potential noninvasive test for overcoming the current barriers in endometriosis diagnosis. **Conclusions.** Various lines of evidence support the potential role of many biomolecules or panels of biomolecule but, for the moment, none of them are showing the proven sensibility and specificity of the test. Therefore, they can only complete the diagnosis of this pathology, alongside imagistic techniques or laparoscopic surgery.

Keywords: endometriosis, biomarker, noninvasive diagnosis, mi-RNA

How to take off the mask of endometriosis...

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Introduction. Endometriosis in its multiple locations (genital and extragenital) may deceive the clinician through the overlapping clinical picture. Most of the patients with severe endometriosis and/or adenomyosis are diagnosed late, after years of unnecessary suffering. **Materials and method.** Concurrent pelvic pathology like ovarian cysts, pelvic inflammatory disease and pelvic varicosities may be misleading. Adenomyosis is frequently associated with endometrial polyps, endometrial hyperplasia or uterine fibroids. Patients with endometriosis suffer simultaneously from irritative bowel syndrome, interstitial cystitis and fibromyalgia. Extrapelvic endometriosis may be sometimes missed (for example, abdominal wall endometriosis). We may observe several

common psycho-behavioral traits of patients with endometriosis. **Results.** Subfertility, infertility and chronic pelvic pain are encountered unfortunately far too often, as a result of delayed diagnosis of endometriosis. The exclusion of clinical, imaging and laboratory criteria for concurrent pelvic, genital, digestive or urinary pathology have to be thoroughly applied. Taking a more detailed history and sketching a psychological profile may improve our diagnostic approach and also the treatment steps which have to be taken. **Conclusions.** A higher degree of clinical suspicion is mandatory in early diagnosis of endometriosis, in whatever localization of the disease.

Keywords: endometriosis, early diagnosis, concurrent pelvic pathology

Septate uterus: diagnosis and treatment

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Introduction. The uterine malformations are caused by deficitary development of the müllerian ducts during the embryological life. With a prevalence of 1-6% in the general population, they result in an abnormal uterine cavity, which has a negative impact on fertility. The most frequent uterine malformations are represented by the septated arcuate and bicornuate uterus and result from an incomplete absorption of the müllerian ducts. Often, the differentiation between these pathologies through imagistic techniques can be troublesome. The new ASRM classification comes with remarks in this regard. The aim of the treatment is the restoration of the uterine cavity, since the reconstruction of the normal uterine anatomy is key to a better reproductive function. **Materials and method.** This poster describes a clinical case of uterine

malformation in a 33-year-old patient with infertility, showing the diagnostic and therapeutic protocol, as well as the impact over fertility. **Results.** Using 3D US and ASRM criteria, the correct diagnosis of septate uterus could be placed. Hysteroscopic resection of the septum and the restoration of the uterine cavity allowed the implantation of an embryo via IVF. **Conclusions.** The treatment gold standard of uterine malformations is represented by hysteroscopy, which has a low risk of post-operative complications and leads to an improvement of the reproductive function. Applying the ASRM criteria, a correct diagnosis can be made with ease, allowing for the most effective treatment protocol to be followed.

Keywords: infertility, hysteroscopy, ASRM, uterine septum

Management of infertility in a patient with stage III endometriosis and poor ovarian reserve

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Introduction. Endometriosis negatively impacts fertility. A combination of surgery, ovulation induction with assisted reproductive technology can help these women to conceive. **Case report.** We present the case of a 29-year-old patient, diagnosed with primary infertility for over four years. At the age of 25, the patient was operated laparoscopic for stage II endometriosis and had one IVF cycle after with one blastocyst transferred and no pregnancy occurred. The evaluation of infertility shows an anti-müllerian hormone of 1.05 ng/ml with antral follicle count 13 and one endometrioma of 37 mm on the left ovary. Considering the poor ovarian reserve, we decided to prioritize the IVF cycle using agonist protocol

with nine oocytes retrieved and two blastocytes cryopreserved. The patient had a laparoscopic surgery for stage III endometriosis, with the excision of bilateral ovarian cysts, adhesiolysis and the excision of peritoneum lesion of endometriosis. Three months later, we performed a frozen single embryo transfer with term delivery of a healthy boy. **Conclusions.** To maintain the ovarian reserve, we decided on IVF with cryopreservation of the embryos before surgery. Because stage III/IV disease negatively impacts the ART outcomes, we proceed with frozen embryo transfer after treating the endometriosis.

Keywords: endometriosis, IVF (*in vitro* fertilization), laparoscopic, ovarian reserve

Computational models for diagnosing and treating endometriosis

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Introduction. Endometriosis is a widespread disease that is yet poorly understandable. Symptoms may start as early as menarche in adolescents and can be devastating. Despite this, patients are possible to suffer for years before receiving a proper diagnosis and treatment care. Understanding the processes by which immunological, hormone and vascular abnormalities occur in endometriosis and complicate medication can be aided by the use of computational models. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis", "computational", "diagnosing" and "treating". Based on the articles of Ahn et al., 2017, Dorien et al., 2019, Ensari et al., 2020, Mbuguiro et al., 2021, Reinecke et al., 2018, and Winzenborg et al., 2018, we tried to find the answers to questions about how computational models can be used to improve the diagnosis and treatment of endometriosis. **Results.** The first endometriosis computational models that have an effect in the clinic were regression models that helped establish non-surgical screening tests for symptomatic women with endometriosis. Regression is a type of machine learning that is essentially data-driven, making predictions based on quantifiable parameters without considering causal linkages. Research has revealed potential endometriosis biomarkers using data from blood, peritoneal fluid, eutopic endometrium and urine, thanks to the advances in the methodology of collecting and analyzing patient

samples. In order to find the links between endometriosis and gene expression regulators, angiogenic factors, growth factors and cytokines, regression modeling was performed. Logistic regression modeling is often used to create clinical scales, detect disease risk factors and provide therapeutic recommendations. The results of logistic regression and associated models have been presented as support for endometriosis diagnostic tools. Pharmacological models are suitable for modeling and comparing multiple dosage levels, regimens and delivery locations for endometriosis medicines. With the development of these models, researchers were able to discover endometriosis patients with a genetic proclivity for a GnRH antagonist, predict changes in bone mineral density and investigate the role of delivery method in the efficacy of progestin treatments. **Conclusions.** The development and refinement of computational models that can take part in diagnosing and treating endometriosis still have a lot of room for improvement. Researchers can integrate multiscale experimental and clinical data to detect endometriosis predictors and develop treatments using a variety of computer modeling tools. Moreover, designing mechanism-based models that explain how abnormalities in cell signaling influence immunological, vascular, hormone systems and eventually lead to endometriosis, is an appealing prospect.

Keywords: endometriosis, computational, diagnosing, treating

Endometriosis – current management and future trends

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Introduction. Endometriosis is a chronic disease that is characterized by the presence of endometrial glands and stroma-like lesions outside the uterus. Until now, treatment approaches involved surgery, assisted therapy or medical therapy. It is crucial to find new therapeutic targets that can increase the chances of pregnancy and improve the quality of life of patients. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis", "management", "future" and "perspectives". Based on the articles by Anastasiu et al., 2020, Chapron et al., 2019, Falcone and Flyckt, 2018, Ferrero et al., 2018, Hirsch et al., 2018, and Parasar et al., 2017, we tried to find the answers to questions about the current management of endometriosis and the future perspectives. **Results.** Endometriosis management necessitates a multidisciplinary strategy that includes surgical diagnosis and debulking of the disease burden, hormonal therapy in order to suppress and postpone disease recurrence and progression, and pain control methods. Endometriosis must be diagnosed early and accurately in order to manage this benign but debilitating condition. A late diagnosis is frequently determined by the lack of particular

symptoms. Invasive surgery followed by a histological examination remains the gold standard, but it must be balanced against the risks of surgical morbidity and possible ovarian reserve reductions. A biomarker or a panel of biomarkers is simple to assess, typically noninvasive, and can provide valuable guidance in both diagnosing and tracking therapy response. Until now, treatment approaches involved surgery, assisted therapy or medical therapy. With the evolution of technology and new research discoveries, new markers have been identified that might be used as new therapeutic targets. **Conclusions.** The management of endometriosis patients is a challenging task. As we get a better understanding of the pathophysiologic mechanisms of endometriosis, we will be able to better identify noninvasive diagnostic approaches and novel therapeutic targets, avoiding in this way the surgical morbidity and the reduced ovarian reserve. Proteomics, genomics and metabolomics which analyze a whole panel of biomolecules and gene profiles might emerge into the gold standard diagnostic tool, obviating any need for invasive laparoscopies.

Keywords: endometriosis, management, future, perspectives

New trends for the medical treatment of endometriosis

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Introduction. Endometriosis is a condition that concerns 10% of reproductive-aged women. It is associated with pain, infertility, and sexual difficulties, leading to psychological problems. Although the gold standard for treatment is surgery, it is a high-cost procedure with significant morbidity. Consequently, the medical treatment has an important role in the management of endometriosis. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis" and "medical treatment". Based on the articles by Angioni et al., 2020, Barbara et al., 2021, Nirgianakis et al., 2020, Reis et al., 2020, Schwartz et al., 2020, Vannuccini et al., 2021, and Vercellini et al., 2018, we tried to examine the new trends for the medical treatment of endometriosis. **Results.** There are conventional and emerging medical treatments for endometriosis. Conventional drugs include progestins, combined oral contraceptives, GnRH agonists/antagonists, nonsteroidal anti-inflammatory drugs and aromatase inhibitors, while emerging medicines focus on disease-specific targets. Currently, hormonal drugs are the most common drugs, targeting endocrine pathogenetic aspects, especially progesterone-resistance and

estrogen-dependency. Sometimes, the efficiency of these drugs is enough to avoid surgery. However, considering that there are high rates of intolerance, it was important to identify the risk factors. These include genital bleeding during dienogest treatment, low stages of the disease, dysmenorrhea before treatment, and suspicion of adenomyosis. In addition, cost-effectiveness analyses are required for a better management, considering that long-term strategies and high-value treatment should be chosen depending the patient's priorities. Furthermore, nowadays there are many clinical trials for emerging medicines. It is important to focus on finding targets that have synergic effects, such as the critical mediator transcription factor promyelocytic leukemia zinc finger (PLZF). **Conclusions.** There are currently many available medicines subscribed for endometriosis, with different advantages and disadvantages. It is crucial to develop a more individualized therapy, considering the patient's symptoms, the desire for pregnancy and the cost burden. In addition, finding novel disease-specific targets is important to achieve a better therapy.

Keywords: endometriosis, medical treatment, medical therapy, drugs

The effect of endometriosis on the quality of life of women

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Introduction. Endometriosis is a chronic inflammatory disease that affects up to 10% of women of reproductive age and can induce symptoms such as dysmenorrhea, dyspareunia and chronic pelvic pain. There is a growing body of research that summarizes the effect of endometriosis on quality of life, including work, relationships, sexual function and psychological aspects. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis", "quality of life" and "women". Based on the articles by Corte et al., 2020, De Freitas et al., 2018, Leuenberger et al., 2022, Marki et al., 2017, Missmer et al., 2021, and Wang et al., 2021, we tried to find the answers to questions about the effect of endometriosis on the women's quality of life. **Results.** Endometriosis-associated pain plays a central role in the poor impact on the quality of women's life. Pain can lead to bad sleep quality, increased stress, limited activity and to a variety of psychological conditions, such as depression and

anxiety. Moreover, the pain might interfere with sexual activities, negatively affecting psychological health, the quality of life and the social relationships. Absenteeism or the inability to work for long periods frequently occurs due to symptoms like exhaustion, mood fluctuations and intense bleeding. During a lifetime, these everyday challenges may translate into restrictions in pursuing educational opportunities, making career choices and fulfilling relationships, all of which ultimately may change the course of one's life. **Conclusions.** Endometriosis is a pathology that has a negative impact on nearly every aspect of a women's life, including basic activities like walking, sleep, sitting, physical exercises, family responsibilities, sexual activity, social stability, work career, emotional state and joy of life. Therefore, it requires a multidisciplinary approach, including not only medical treatment, but also psychological, occupational and financial assistance.

Keywords: endometriosis, quality of life, women

New approaches to the use of animal models in the study of endometriosis

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Introduction. Endometriosis is a chronic disorder that remains poorly understood. There is a crucial need for understanding the pathogenesis of the disease and to find new treatments. Animal models are an important tool for revealing the etiology and for examining possible treatments. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis" and "animal models", for the last five years. Based on the articles by Abdolmaleki et al., 2021, Bruner-Tran et al., 2018, Gu et al., 2020, Laganà et al., 2018, Malvezzi et al., 2020, Simitselidis et al., 2018, and Taniguchi et al., 2021, we tried to examine the use of animal models in endometriosis. **Results.** Animal models for endometriosis include rodent animals and non-human primates. Rodent models are mostly rats or mice models, syngeneic or xenotransplant. These models are an important tool for studying the immune system and hormone changes, pathogenesis mechanisms, and testing for new therapies. For example, knockout and transgenic murine models are useful for understanding the immune changes. Furthermore, mice that ex-

press a green fluorescent protein (GFP) can elucidate the disease mechanisms. A new potential rat to mouse model includes xenograft transplantation of endometrium from rat to anterior abdominal wall of mice. In addition to endometriosis-induced rodent models, some primates can develop endometriosis spontaneously, like rhesus monkeys and baboons (*Papio anubis*). However, endometriosis-induced models have been developed for other primates too, such as cynomolgus monkeys (*Macaca fascicularis*). Non-human primate models may have a biological response closest to humans, although bioethical reasons and high costs have limited their use. Additionally, there are inconsistencies from disease experimental models to clinical trials. **Conclusions.** Animal models are a useful tool for unraveling pathogenic mechanisms and for finding new therapies for endometriosis. Transplantation can lead to molecular, histological and genetic characteristics similar to humans. However, many clinical trials of drugs fail in humans, suggesting that is important to develop new models.

Keywords: endometriosis, animal models, rodent models, primate models

Uncovering the genetic basis of female infertility and endometriosis

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Introduction. Endometriosis is a pathological condition associated with infertility. Many studies are aiming at understanding the genetic profile of endometriosis in order to identify novel management and treatment approaches. **Materials and method.** A recent literature search was conducted on the basis of PubMed, using the keywords "endometriosis", "genetics" and "infertility". Based on the articles by Almasi et al., 2021, Amirteimouri et al., 2019, Araujo et al., 2017, Ashary et al., 2020, Balasubramanian et al., 2018, Bianco et al., 2019, and Vassilopoulou et al., 2019, we tried to find the answers to questions about the genetic basis of endometriosis and its effects on infertile women. **Results.** Many genes and polymorphisms are involved in endometriosis. Cellular cycle-, proliferation- and apoptosis-related loci, detoxification genes, inflammation and autoimmunity-related genes, angiogenesis-related genes and hormonal function genes have been associated with endometriosis. Hoxa-10 is an important gene that is correlated with endometriosis, especially in infertile women.

Another recent study has proven that the expression of IL-6 and IL-8 cytokines and other genes in the TLR3 cascade are upregulated in women with endometriosis. Furthermore, an important tool in the regulation of cell proliferation genes is the inhibitor of differentiation (ID) family. The nuclear transcription factor Y (NF-Y) regulates ID via CCAAT box region, suggesting a possible role in epigenetic changes of the endometrium. Another recent investigation revealed that ID2, PRELP and SMOC2 genes express differently in women with endometriosis. Recent papers also suggest that STAT4 polymorphisms are linked to endometriosis. **Conclusions.** There is a strong correlation between genetic evidence and endometriosis. Many genes are associated with the pathogenesis of endometriosis. A better understanding of the difference in the genetic profile is important to understand the pathogenesis and for finding new biomarkers for diagnosis and novel targets for treatment.

Keywords: endometriosis, genetics, genetic polymorphism, infertility

Beyond the uterus and ovaries. Transvaginal ultrasound as the first line of diagnosis in deep infiltrative endometriosis

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Endometriosis is a benign condition with high incidence and with an overall diagnostic delay of up to eight years. This delay is caused by multiple factors: COC treatment, symptomatic treatment of dysmenorrhea, the lack of awareness both in the general population and in the medical community. The diagnostic delay refers to the period between the onset of symptoms and the diagnosis of the first lesion. One good question is: what is the diagnosis delay of deep infiltrating endometriosis lesions in patients with endometrioma and adenomyo-

sis? Although the ultrasound is an effective diagnostic tool for deep infiltrating endometriosis and for preoperative planning, it is still not used widely enough in clinical practice as the first-line imaging method. A good characterization and mapping of endometriotic lesions can help us refer patients to centers of excellence in endometriosis, where advanced cases may be treated with minimally invasive surgery.

Keywords: transvaginal ultrasound, endometriosis, first-line diagnosis

KIR-HLAC genotyping can assess the human reproductive success

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Introduction. KIR-HLAC (Killer Immunoglobulin-like Receptor-Human Leukocyte Antigen-C) genotyping is a genetic test that allows the determination of allelic variants C1 and C2. Together with KIR genotype, this test helps to establish the risk of an altered maternal immune response to embryos. **Case report.** We present the case of a couple with primary infertility for two years. The female partner is 34 years old, AMH (anti-müllerian hormone) 5.12 ng/ml and bilateral tubal patency, and her partner has normospermia. After an intrauterine insemination failure, we decided on an IVF (*in vitro* fertilization) cycle using an antagonist protocol, in which 11 oocytes were retrieved, five blastocysts obtained and one single fresh embryo transfer performed, but no pregnancy occurred. The couple continued with more

investigations, with peripheral blood lymphocytes NK (natural killer) 25%, positive Hidden C test for *Chlamydia* and treated, normal endometrial receptivity, and normal couple genetic karyotype. KIR-HLAC genotyping revealed an HLA-C genotype C1/C2 with KIR genotype AA and HLA-C C1/C2 for the male partner. This genotype is associated with an increased risk of implantation failure and pregnancy complications. The patient had three frozen embryo transfers, but no pregnancy occurred. **Conclusions.** In repeated implantation failure, it is important to start the investigations of the maternal immune system, in order to adapt the protocol of the assisted reproductive treatment.

Keywords: repeated implantation failure (RIF), KIR, HLA-C, IVF, infertility

Fertility management in patients with severe endometriosis

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As more and more couples face infertility, one of the most challenging causes is represented by endometriosis. Latest studies have shown that more than 10% of reproductive-aged women suffer from endometriosis. The pathogenesis of endometriosis can offer some insight for what exactly the mechanism for infertility is. The management of the patient include a specific balance

between pain management, fertility management and quality of life improvement. The aim of this presentation is to discuss the current approaches to endometriosis-related infertility, especially in severe endometriosis in need for extensive surgery.

Keywords: endometriosis, fertility, fertility sparing surgery

First laparoscopy or IVF in endometriosis with infertility

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Laparoscopic surgery can improve pregnancy rates not only for minimal and mild disease, but also for more advanced endometriosis. There is one reason why laparoscopic surgery is less commonly employed today than it has been in the past: higher success rates with IVF. Therefore, IVF would seem to be a preferable alternative to repeat surgery for most patients. We suggest to treat large endometriomas more 3 cm, especially if the response to ovarian stimulation drugs is poor before surgery. We perform operative laparoscopy (excision or ablation of the endometriosis lesions), including adhesiolysis, rather than laparoscopy only, to increase ongoing pregnancy rates. However, such surgery can be very difficult and requires a talented surgeon in order to avoid vascular and ovarian injury that might result in even poorer ovarian response postoperatively. The decision to operate is not easy. We report the increased diagnostic accuracy of laparoscopy in endometriosis using indigo

carmine. Counseling regarding the risk of reduced ovarian function after surgery and the possible loss of the ovary is necessary. The optimal approach to managing the infertile endometriosis patient is to perform a comprehensive evaluation, and then develop a treatment plan that progresses from simpler, yet effective and safe, treatments to more complex and costly treatments. The major advantage of IVF is the fact that it treats multiple infertility problems of both the female and male, has a high rate of success on just one attempt relative to surgery, and takes only 2-3 months to complete the treatment, making it more attractive for older patients. We believe that the subset of patients who have failed multiple cycles of IVF may harbor a certain type of endometriosis which allows them to benefit from thorough surgical therapy.

Keywords: endometriosis, laparoscopy, infertility, IVF

A rare case of thoracic endometriosis syndrome

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Introduction. Among women diagnosed with endometriosis, 12% are estimated to experience endometriosis of nonreproductive organs, referred to as extragenital endometriosis. The most common site of endometriosis outside of the abdominopelvic cavity is within the thoracic cavity. Endometriosis within the lung parenchyma or on the diaphragm and pleural surfaces produces a range of clinical and radiological manifestations, including catamenial pneumothorax, catamenial hemothorax, catamenial hemoptysis and pulmonary nodules. Collectively, this is known as thoracic endometriosis syndrome (TES). **Materials and method.** The presentation is structured in two parts. After a short review of the literature, we present the case of a 32-year-old

female with heavy vaginal bleeding, chest pain and cough. **Discussion.** Although the pathogenesis of thoracic endometriosis is not yet fully understood, several theories have been presented. As none of the theories alone can account for all clinical manifestations of the syndrome, the etiology of TES is still unclear. It is also a pathology that is difficult to diagnose because it can mimic other diagnostics and the incidence of cases is very low. The management of these cases is extremely difficult, because the quality of the patient's life and the invasiveness of the recommended procedures must be permanently weighed.

Keywords: extragenital endometriosis, catamenial pneumothorax, thoracic endometriosis syndrome

Clear cell carcinoma in ovarian endometriosis: a not so rare malignancy arising at a very uncommon age – case report and literature review

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Introduction. Ovarian cancer is the most common cause of cancer death worldwide. The incidence of ovarian cancer is higher in postmenopausal women. Endometriosis is common and found in about 10% of reproductive-age women, but the risk of malignant transformation in an individual patient is very low. Nonetheless, endometriosis is associated with up to 20% of ovarian cancers and is acknowledged to be the precursor of most endometrioid, clear cell, and seromucinous carcinomas. The relative proportion of endometrioid and clear cell carcinomas that are associated with endometriosis is much higher than that for the other cell types. **Materials and method.** We present the case of a 28-year-old female who presented in our medical unit for acute pelviabdominal pain associated with moderate leukocytosis. MRI showed a solid and cystic mass, associated with ascites, heterogeneous in T1-weighted sequence and hyperintense in T2-weighted sequence. Based on the clinical findings, we opted for a fertility sparing approach and unilateral ovariectomy was performed, followed by biopsies of the parietocolic fossae, great omentum and lomboarctic lymph nodes. **Results.** Gross examination revealed a large ovarian mass, with

intact capsule, measuring 10/8/7.5 cm, showing a predominantly cystic structure filled with red-brown liquid and unremarkable internal surface except for a solid area measuring 8/7/4 cm, with friable consistency and diffuse grey-yellow color. The histopathological examination revealed a predominantly diffuse proliferation of polygonal cells with clear cytoplasm with PAS-positive material and hyperchromatic nuclei, arising in the setting of an endometriotic cyst. The immunohistochemical examination revealed diffuse positivity for CK7, PAX8 and Napsin A, consistent with the diagnosis of clear cell carcinoma. Inhibin, WT1, OCT4 and CD117 were diffusely negative. **Conclusions.** Although clear cell carcinoma occurring in the setting of an ovarian endometriotic cyst is a relatively common occurrence, its presence in a female below 30 years old is extremely rare. In this case report, we highlight the importance of prudent clinical and pathologic examination, since the misdiagnosis of such lesions may lead to erroneous therapeutic management and can lead to an unfavorable long-term outcome.

Keywords: clear cell carcinoma, endometriosis, ovarian cancer

Is there success in pursuing novel treatment options for women with endometriosis?

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Endometriosis is a widespread gynecological disease that continues to be a significant clinical challenge to diagnose and treat. At present, the disease management may include the surgical excision of ectopic endometriotic lesions or surgical ablation of more superficial lesions and the hormonal suppression of menstruation and ovarian function. Sadly, there is a high recurrence rate for both interventions; thus, women who wish to conceive remain with the choice between achieving pregnancy and managing their pelvic pain. In the pursuit of novel treatment options for women with endometriosis, melatonin displayed potentially beneficial effects in estrogen-dependent diseases. Latest years studies revealed that melatonin receptors, MR1A and MR1B, are present in epithelial cells of endometrial glands through-

out the menstrual cycle. The eutopic endometrium and ectopic lesions of women with endometriosis expressed MR1A and MR1B mRNA and protein. Physiologically relevant melatonin concentrations inhibit estradiol-induced proliferation of endometrial epithelial cells in culture. Current data demonstrate that the endometrium and endometriotic lesions possess an intact melatonin receptor signaling pathway and that melatonin inhibits estradiol-induced cell proliferation. Melatonin also modulates endometrial epithelial cell function and antagonizes estrogen-driven proliferation of ectopic endometrial tissues, demonstrating beneficial effects on endometriosis management.

Keywords: endometriosis, novel treatment, melatonin

Parietal endometriosis: a challenging disease

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Parietal endometriosis is a fairly rare condition which usually develops in women after obstetrics-gynecological procedures or surgery. Although some cases are asymptomatic, many patients accuse symptoms such as chronic abdominal pain with or without palpable mass and significant exacerbations of this during menstruation. The diagnosis is based on the patient's medical history that reveals a caesarean section or another gynecological surgery in the past, as well as the results

of imaging investigations. Managing this condition is challenging and requires close multidisciplinary collaboration between radiologist, gynecologists and surgeons, especially in patients who need complex surgical procedures. The aim of our paper is to present the risk factors, the clinical and paraclinical diagnosis, as well as the therapeutic management of this challenging disease

Keywords: abdominal endometriosis, endometrioma, parietal endometriosis, chronic abdominal pain

The endometriosis patients' quality of life – how can it be evaluated and improved?

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Introduction. Endometriosis is the gynecological pathology that affects women's health and quality of life because of the symptoms, repeated surgical procedures and the long-term consequences. The surgical approach represents a challenge even for experienced surgeons in specific endometriosis centers. **Materials and method.** We evaluated the international databases using the keywords "questionnaire", "endometriosis", "laparoscopy", "medical approach" and "quality of life". We selected the studies about endometriosis with laparoscopic and medical approach from beginning to March 2022. **Results.** There were identified 62 studies that met the criteria. The main questionnaires for quality of life and endometriosis are the generic Short Form Health Survey and the Endometriosis Health Profile 30, Short Form Questionnaire SF-36, and the pain questionnaires, such

as the Pain Catastrophizing Scale (PCS) scale and the verbal Numeric Rating Scale (NRS). Studies revealed that women with endometriosis have no correlation between symptoms and the severity of the lesion. The pathology profoundly affected their quality of life. The characteristic of pain imposes surgical approach. Patients with endometriosis also experience anxiety that may require psychological support. **Conclusions.** Laparoscopic approach represents the optimal therapeutic option for endometriosis, but medical therapy can improve quality of life in selected cases. The quality-of-life questionnaires demonstrated that endometriosis symptoms and quality of life may be positively changed after medical or surgical therapy.

Keywords: quality of life, endometriosis, laparoscopy, SF-36

Practice points in cervical precancer detection

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During daily consultations of asymptomatic women, all gynecologists have to make decisions regarding the prevention or management of cervical precancers, either by recommending further investigations, performing colposcopy themselves or acting upon various testing results brought in by their patients. Choosing the appropriate attitude and adapting the international protocols are often demanding tasks throughout the current transition time from the free conventional cytology to a broader range of new screening and triage assays and technologies. Despite these significant recent developments in screening testing, colposcopy still represents the core and basis of cervical precancer management. The accuracy of the histological diagnosis depends on the expertise of the colposcopist in providing punch, endocervical or excisional biopsy specimens. A multidisciplinary team specialized in cervical pathol-

ogy from Micomi Clinic, Bucharest, will debate and illustrate alternative answers to the clinical dilemma "What to do when...", covering several common practical management issues, like unsatisfactory cytology and HPV results, HPV positive/negative cytology, HPV negative/positive cytology, positive cytology/negative colposcopy with type 1, 2, 3 TZ, endocervical brushing, the significance of the "test of cure", and triage of HPV positives by biomarkers. Several colposcopy cases will be also presented to allow the clinical and pathological contexts, like new versus persistent HPV infections, immunomodulatory treatment versus non-treatment in productive HPV infections, and conservative follow-up versus interventional management in HPV-positive women.

Keywords: colposcopy, pathology, cytology, HPV testing, biomarkers

New evidence on efficacy of one-dose human papillomavirus (HPV) vaccine against cervical cancer

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Cervical cancer, often referred to as the "silent killer", almost entirely preventable, is a disease of inequity of access. More than 95% of cervical cancer cases are caused by sexually transmitted HPV and represent the fourth most common type of cancer in women globally. Unfortunately, 90% of these women live in low- and middle-income countries. According to newly emerged data from the World Health Organization (WHO) on the efficacy of HPV vaccine, it appears that a single-dose schedule is comparable to two-dose or three-dose

regimens. This could be a game-changer for disease prevention, considering that more doses could reach a larger population, especially for women living in poorer countries. Ultimately, there is not enough evidence regarding the efficacy of single-dose vaccination in immunocompromised individuals, thus they should receive three doses or at least two doses if the first option is not feasible.

Keywords: anti-HPV vaccine, one-dose vaccine, cervical cancer

The HPV vaccine – between social media myth and reality

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Human papillomavirus (HPV) infection is known to be sexually transmitted and can range from benign lesions (genital warts) to anogenital and oropharyngeal cancer. Every year, in the United States of America, more than 30,000 people are diagnosed with HPV-associated cancer, and vaccination could prevent about 90% of these cases. Among the cancers that are associated with HPV, the only type that can be diagnosed by routine screening is cervical cancer, with the rest of the malignancies being detected after the development of symptoms. The combination of regular screening and HPV vaccination is the main strategy used to eliminate cervical cancer, the latter being recommended by WHO starting with 2014 to be administered to all adolescents aged 9 and older. With the beginning of HPV vaccination campaigns around the world, parents have become less interested in vaccinating their children, possibly due to a lack of

concrete information about the vaccine, adding to the possible danger to which the child is exposed as an adult in case of contracting the virus. A number of realities related to the HPV vaccine could be debated in the general population, including the fact that this vaccine is recommended for both boys and girls, that it is a safe vaccine in terms of effectiveness, that it prevents a series of cancers caused by HPV, that children can benefit from this type of vaccine free of charge through the national vaccination program, that it also does not affect fertility, and so on. In order for a vaccination campaign to have a positive impact on the general population, it is necessary to address the correct and comprehensible information to the beneficiaries that vaccination can bring, both by eliminating false information and by spreading the details of the vaccine as widely as possible.

Keywords: HPV vaccine, media, cervical cancer

The value of cytotumor examination in the diagnosis of dysplasia and cervical cancer. The new approach to cervical screening

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Cervical cancer represents an important cause of morbidity and mortality, being the most frequent neoplastic disease among women in most countries. The screening of this pathology is considered one of the most efficient prevention programs of malignancies. The introduction of the Pap smear test was associated with both the reduction of the incidence and mortality from cervical cancer. With the discovery of the human papillomavirus and its carcinogenic potential, a new era in terms of screening and prevention has begun. The new trends adopted in some developed countries propose a primary HPV test alone every five years, starting at the age of 25 years old or, as an

alternative, the co-testing, Pap smear test and HPV test, every five years, or the Pap smear test alone every three years. Women aged over 65 years old should consider to stop screening only when they have two consecutive negative primary HPV tests or co-tests or three negative cytology tests in the past 10 years, the most recent done within the past 3-5 years. The main objective of this study is to evaluate the value of cervical smear measured according to its correspondence between the biopsy result and histopathological conization or hysterectomy exam.

Keywords: cytotumor examination, cervical cancer, cervical screening

Colposcopic findings among women with high-risk HPV

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Introduction. In 2020, the American College of Obstetricians and Gynecologists (ACOG) updated the guidelines for the management of cervical cancer screening abnormalities. Taking into consideration that HPV 16 or 18 infections have the highest risk for CIN 3 and occult cancer, additional evaluation (e.g., colposcopy with biopsy) is necessary even when the cytology results are negative. If HPV 16 or 18 testing is positive, and additional laboratory testing of the same sample is not feasible, the patient should proceed directly to colposcopy. **Materials and method.** Taking into account the new recommendations, colposcopies were performed in patients aged 24-65 years

old with HPV 16 and/or 18 infection. **Results.** The colposcopy aspects vary considerably in the case of the same type of HPV. There are cases of HPV 16 with almost no abnormal aspect in colposcopy, and cases of CIN3 or HSIL in which the aspect of the cervix contains all the modifications described in literature. **Conclusions.** Colposcopy is considered to be the tool with which we can diagnose macroscopically a preinvasive lesion of the cervix. The only problem is that the variety of aspects for each type of HPV is overwhelming, making the clinician's job hard if he or she doesn't corroborate all the investigations.

Keywords: colposcopy, HPV 16, HPV 18

Clinical and virological risk factors involved in premalignant and malignant lesions of the uterine cervix – particular features in Romanian patients

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Introduction/objectives. Romania ranks first regarding the incidence and mortality of cervical cancer (CC) in the European Union. The persistent infection with high-risk HPV subtypes is a confirmed precursor in the development of almost all invasive cervical cancers, with HPV 16 and HPV 18 being classically considered the most common oncogenic subtypes. The prevalence of various HPV strains varies widely across the globe. The objectives of this study were to determine the presence of HPV infection and the infectious viral subtype in patients with normal cervix, CIN and with cervical cancer hospitalized in our institution, as well as to evaluate the particularities of this infection according to certain clinical parameters, in order to prioritize the screening services for patients with high-risk characteristics for HPV-induced disease in our geographic region. **Materials and method.** A total of 77 patients admitted to the "Dominic Stanca" Clinic of Obstetrics and Gynecology, Cluj-Napoca, were enrolled in the study, grouped in three categories: Group 1 – Control (n=38), Group 2 – CIN (n=30), Group 3 – CC (n=9). For all patients, the diagnosis of the cervical condition was confirmed by histopathological examination. A complex clinical database was developed, followed by the detection of high-risk HPV strains by the HPV Genotypes 14 Real-TM Quant kit. The number of previous cyto-tumoral examinations, as well as the macroscopic appearance of the cervix at the gynecologic examination were also recorded. The SPSS v. 24.0 pro-

gram was used for data analysis, considering the statistical significance at the standard level of 5%. **Results.** HPV infection was detected in 88.3% of the subjects and a large number of patients were coinfecting with several HPV strains. The most prevalent HR strains were HPV 16, 58, 56, 52, 33 and 31. Considering a single examination, 42% of patients in the control group had abnormal cytological results (PAP III, PAP IV), probably in association with the presence of the HPV infection; however, all patients (100%) in CIN and CC groups had abnormal cytology. At the clinical examination, 26.3% of patients without neoplastic cellular changes had a cervix presenting a macroscopic lesion. When analyzing the appearance of the cervix according to the HPV status, it was found that almost half (44.11%) of the patients with microscopically normal cervix had HPV infection, in 96.8% of cases the detected strain being HPV 16. **Conclusions.** This study highlighted HPV 16, 58, 56 and 52 as the most prevalent strains in the analyzed population. Given the wide variability in the prevalence of HPV-HR strains by geographical area, it is important to include the most common genotypes in the test kits for each region. The appearance of a cervical lesion is associated in half of the cases with HPV 16 infection, in case of normal cytology. HPV testing could bring additional benefits in guiding the subsequent management for these patients.

Keywords: cervical cancer, cervical intraepithelial neoplasia, human papillomavirus, risk factors

Residual disease and/or CIN 2-3 recurrence – the practical approach

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Introduction. HPV-induced pathology remains a great challenge for current gynecological practice. High-risk HPV types are involved in severe intraepithelial lesions and we observe such lesions in more young patients, which have not completed their reproductive plans. For clinician, it is of utmost importance to maintain a fair balance between excessive and incomplete treatment. **Materials and method.** The incomplete excision of a high-grade cervical lesions is recognized to be the most important predictive factor for residual and/or recurrent disease. We perform large loop excision of the transformation zone (LLETZ) when the lesion is entirely visible at colposcopy or conization (electric or cold-knife conization) when the lesion is incompletely visible. The positive margins of the excised high-grade

specimen seem to be the most valuable predictor of residual disease. **Results.** Age, parity, lesion grade, HPV type and positive margins are predictors of residual disease and/or of CIN 2-3 recurrence. Some differences are observed regarding the type of excision. Probably due to the reparatory effect after LLETZ or electric conization, post-excisional cytology at four to six months tends to be negative or low-grade, as well as the result of HPV testing. Parakeratosis or keratosis are important cytological features in the follow-up. Colposcopy surveillance make sense when trying to avoid reintervention. **Conclusions.** Overtreatment or delayed treatment are pitfalls to avoid in high-grade HPV induced cervical pathology.

Keywords: HPV, residual disease, CIN 2-3 recurrence

Adjuvant HPV vaccination in the prevention of recurrent HSIL lesions after electro-surgical treatment

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Background. Women who have been treated for HSIL lesions have an increased risk of recurrence and cervical cancer. The probability of recurrence depends on the grade of dysplasia, the persistence of HR-HPV and on the woman's age. Limited data show that HPV vaccination at the time of surgical treatment reduces the recurrence risk. **Objective.** To evaluate the efficacy of the non-avalent HPV vaccination in women with HSIL lesions who will undergo electro-surgical treatment preventing HSIL lesions after 24 months. **Materials and method.** Between 2018 and March 2020, we performed 72 loop electro-surgical excision procedure (LEEP) and conization with histologic diagnosis of HSIL. There were two groups: the vaccination group (19 patients) who received three injections with nonavalent HPV vaccine (the first dose at one month before or after surgical treatment),

and the non-vaccination group (53 patients). Women had surveillance with cytology and colposcopy at 3, 6, 12, 18 and 24 months, and HPV test at 6 and 18 months. A normal Pap smear with negative HR-HPV test serves as surrogate for the absence of HSIL lesions. **Results.** One patient (5.2%) in the vaccination group and seven patients (13.2%) in the non-vaccination group developed recurrence. The patients were infected with HPV 16, 33, 45 and 58. **Conclusions.** HPV vaccine can be used in the prevention of recurrent HSIL at the time of surgical treatment. The persistence of HR-HPV is associated with the development of recurrent HSIL and can be reduced using the combination of HPV vaccination and surgical treatment.

Keywords: HR-HPV, LEEP, conization, vaccination, recurrent HSIL

The role of microbiome in persistent HPV infection

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Introduction. Bacterial vaginosis is an important affliction. The mechanism may be an increase in mucin degradation enzyme in vaginal fluid in patients with bacterial vaginosis which promotes virulence by disrupting mucosal protective barriers, resulting in increased HPV infection through viral adhesion, invasion and HPV genome integration. **Materials and method.** The analysis of the relationship between the vaginal environment and HPV to regulate vaginal microecological balance, block HPV infection and intervention in the prognosis of cervi-

cal lesions. **Conclusions.** Bacterial vaginosis (mycoses, mycoplasmas, *Chlamydia*) and reduced lactobacilli are associated with an increased risk of HPV infection and with the development of CIN. This study shows that vaginal microecological imbalance and weakened local cervical immune function are reasons for the development of cervical lesions. The association of bacterial vaginosis with HPV can be seen. The prevalence of HPV is high in patients with bacterial vaginosis.

Keywords: bacterial vaginosis, HPV, cervical lesions

Societal costs and economic burden of the frail HPV vaccination policy – a Romanian reality

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Cervical cancer and cervical dysplasia remain a global issue, with more than 90% of cervical cancer cases caused by human papillomavirus (HPV) infections. Persistent HPV infection drives dysplasia which, if uncured, can lead to cervical cancer. The Papanicolaou smear is responsible for screening a patient for abnormalities such as cervical dysplasia, thus decreasing cervical cancer incidence and mortality rates. Recent developments in primary prevention include vaccinations against specific strains of HPV and the psychoeducation of the public. Social determinants of health and social factors besides medical care that impact individual and population health indices, including barriers to healthcare access and inappropriate understanding of screening and prophylaxis policies, have been shown to affect cervical cancer screening rates, cervical cancer burden, and

disease attributes. Cervical cancer is the fourth most common cancer among women globally. The burden faced by low- and middle-income countries is significantly greater than in case of high-income countries, and the disparity directly results from the differences in resources. The developed nations have organized vaccination and screening programs that have decreased the cervical cancer incidence. Developing primary and secondary prevention programs and addressing the barriers involved in countries with low socioeconomic levels can drastically reduce morbidity and mortality rates associated with cervical cancer, thus reducing the burden associated with this gynecological malignancy.

Keywords: economic impact, cervical cancer, human papillomavirus, primary prevention, psychoeducation, screening, vaccinations

Antiviral interventions for HPV: current challenges and options

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The infection with the human papillomavirus (HPV) has been proven to cause virtually all cases of premalignant and malignant lesions of the cervix. Current treatment involves surgical and ablative methods which are associated with subsequent morbidity and with the risk of recurrence. This leaves a wide therapeutic gap to be filled in order to achieve better and more durable results in fighting this disease. Current directions of antiviral intervention include prophylactic and therapeutic vaccines, immunotherapy for cervical cancer, and antiviral medication targeting specific HPV proteins. Some of the challenges in developing such strategies come from choosing the best therapeutic target, the lack of appropriate animal models and securing funding for testing new concepts. Prophylactic vaccines have been available for more than 10 years and have shown great efficacy, but they

only cover 15% of the target population so far and do not address the preexisting infection. There are many potential directions for therapeutic vaccines, including using a modified Vaccinia virus or DNA synthetic plasmids of E6 and E7; however, the results are variable and no product has yet been approved. Immunotherapy is a promising concept in treating cervical cancer, but many clinical trials are needed. Most current antiviral directions target HPV 16 and 18 oncoproteins E6 and E7 using a variety of methods: antisense RNA, nucleosidic analogues, CRISPR and green tea extract, yet all require further research and trials. Our aim here is to review the current progress in the research and development of cervical cancer and HPV antiviral intervention and to highlight the need for investing more resources in this topic.

Keywords: HPV, antiviral, HPV vaccines

Vaccination after surgical treatment for CIN

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The infection with the human papillomavirus (HPV) has been proven to cause virtually all cases of premalignant and malignant lesions of the cervix. Prophylactic anti-HPV vaccines have shown great efficacy, but there are many women in the age group of 26-45 years old not yet vaccinated; at the same time, anti-HPV vaccines do not address preexisting infection. Current treatment of human papillomavirus-induced cervical lesions involves surgical and ablative methods. In the vaccinated population, after an excisional procedure, prophylactic anti-

HPV vaccines offer protection against the occurrence of subsequent genital lesions. In the non-vaccinated population, prophylactic anti-HPV vaccination after an excisional procedure offers protection for the risk of recurrent CIN2+, when compared with the group without vaccination. HPV vaccination after the surgical treatment of CIN2+ is a preventive option for subsequent or recurrent genital lesions.

Keywords: HPV vaccines, conization, CIN2+, vaccination after treatment

Genital HPV keratotic lesions – differential diagnosis based on dermoscopic findings

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Introduction. Keratotic lesions are a common encounter in the genital area in the practice of gynecologists or dermatologists. Making a precise diagnosis can be challenging, but it is critical for treatment and prognosis. In these instances, a dermoscopic examination is particularly useful because it is a quick, inexpensive, noninvasive and sensitive examination. However, dermoscopic data comparing bowenoid papulosis (BP), seborrheic keratosis (SK) and *condyloma acuminatum* (CA) is still lacking. More than 40 different genotypes of HPV infect the vaginal area and cause diverse intraepithelial neoplasms. **Materials and method.** We propose to exemplify the differences of the three diagnostics – BP, genital SK and CA – by describing their dermatoscopic characteristics and the relation with the HPV infection. **Results.** Dermoscopic findings: BP has glomerular

vessels, CA has hairpin vessels, and SK has the smallest vascular pattern. The SK has a cerebriform look, while the CA has a knob-like or finger-like shape with a whitish halo. HPV DNA detection is positive in both BP and CA, while studies suggest that more than half of SK have positive HPV findings. BP has the highest detection rate for high-risk genotypes, mostly HPV 16, and CA has the highest detection rate for low-risk genotypes, primarily HPV 6 and HPV 11. **Conclusions.** Before resorting to an invasive procedure, dermoscopy can help distinguish the entity of genital keratotic lesions, and a physician should examine the morphologic plasticity of HPV-related keratosis in the genital area or the genital wart in the enlarged notion.

Keywords: bowenoid papulosis, seborrheic keratosis, *condyloma acuminatum*, dermoscopy

Urinary HPV DNA testing – the method of increasing cervical screening

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Every year, over 1800 women die in Romania as a result of cervical cancer and up to 3,400 are newly diagnosed with this pathology. The incidence is 2.5 times higher than the European average, and the mortality rate is over four times higher, placing us in the first place in terms of incidence and mortality associated with cervical cancer. Thus, there is a need to improve both the primary prevention of HPV vaccination and the screening with an

emphasis on the screening strategy with primary testing of persistent HPV infection. According to multiple recent studies, due to the noninvasive nature and the potential for self-administration, including at home, HPV DNA testing tends to be a screening method appreciated by patients, in contrast to those that postpone the visit to the gynecologist due to psychological considerations.

Keywords: HPV, screening, cervical cancer

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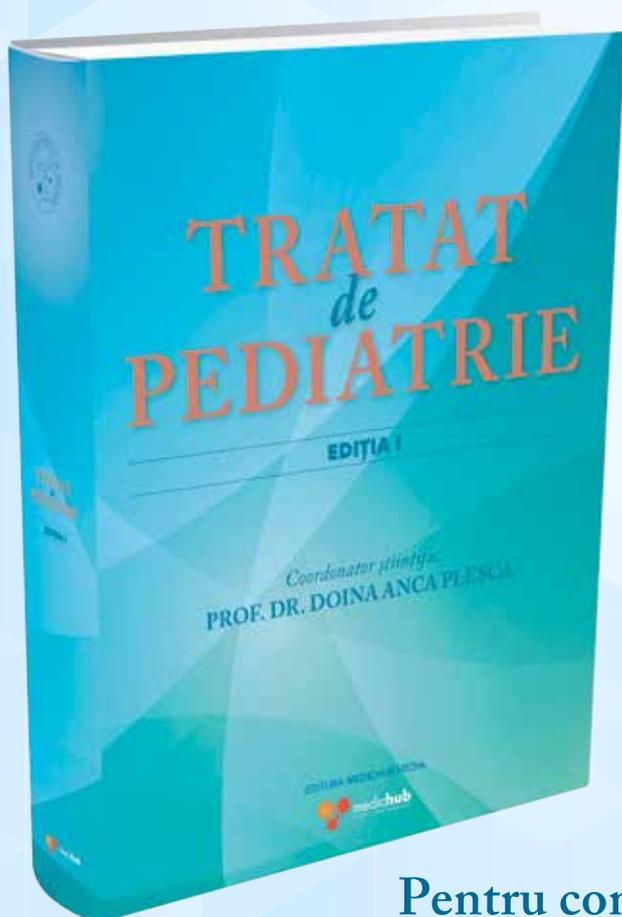
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