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OF THE 8<sup>TH</sup> EDITION  
OF GINECOLOGIA.RO FORUM  
AND THE 4<sup>TH</sup> EDITION  
OF PERINATOLOGIA FORUM

• Bucharest, Romania, March 25-27 2021 •

Societatea Română  
de Obstetrică  
și Ginecologie



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SUPPLEMENT



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## SUMMARIES OF THE 8<sup>TH</sup> EDITION OF GINECOLOGIA.RO FORUM, BUCHAREST, ROMANIA, MARCH 25-27 2021

<b>COVID-19 in pregnancy: the endothelial cell as the target cell .....</b>	<b>8</b>
Alexandru Florin Anca, Andreea Constantin, Corina Grigoriu, Anița Dudău, Lucica Vișan, Alexandru Badiu, Doru Câmpean	
<b>Current treatment options for women with pelvic organ prolapse .....</b>	<b>8</b>
Diana Badiu, Vlad I. Tica	
<b>Possible complications which can appear from using intrauterine devices .....</b>	<b>8</b>
Magdalena-Andra Bălan, A.F. Anca, Gina Ionescu-Anculete, Lucica Eddan Vișan, Alice Negru, Miruna Mînzală, Anita Florina Dudău, Oana Mariana Murgeanu, Corina Grigoriu	
<b>Conservative management of caesarean scar pregnancy using uterine artery embolization .....</b>	<b>9</b>
Roxana Bohîlțea, Bogdan Dorobăț, Ionița Ducu, Bianca Mihai	
<b>Proposals for national improvement of screening and early diagnosis for genito-mammary malignancy .....</b>	<b>9</b>
Roxana Bohîlțea, Florentina Furtunescu	
<b>Rare cases of maternal pathology associated with pregnancy .....</b>	<b>10</b>
Roxana Bohîlțea, Caliopia Parfene, Emilia Niculescu Mizil, Ionița Ducu, Bianca Mihai	
<b>Spontaneous rupture of the internal iliac artery after pelvic radiotherapy – case report .....</b>	<b>10</b>
Andreea Boiangiu, Oana Solomon, Radu Vlădăreanu, Georgiana Bolocan, Andrei Trăistaru, Vlad Zamfirescu, Alexandru Filipescu	
<b>Progesterone priming in controlled ovarian stimulation .....</b>	<b>11</b>
Alina-Elena Bordea, Mihaela Braga, Ioana Iordache, Cristiana Odukoya, Elvira Brătîlă, Andreea Carp-Velișcu	
<b>Benefits of alpha-lipoic acid in high-risk pregnancy .....</b>	<b>11</b>
Mihaela Boț, Ioana Gabriela Calo, Andreea Borisavlschi, Mihaela Bicer, Teodor Bajeu, Mona Elena Zvâncă, Aida Petca, Radu Vlădăreanu	
<b>A new approach to polycystic ovary syndrome .....</b>	<b>11</b>
Mihaela Braga, Alina Bordea, Ioana Iordache, Cristiana Odukoya, Elvira Brătîlă, Andreea Carp-Velișcu	
<b>The impact of the association of maternal HIV infection with IUGR and premature birth on the neonatal outcome – case presentation .....</b>	<b>12</b>
Anca Burnei-Rusu, Vlad Zamfirescu, Andrei Trăistaru, Theodora Ștefania Mardale, Andra Maria Lorentz, Simona Popescu, Radu Vlădăreanu	
<b>Stillbirth in COVID-19 confirmed pregnancies .....</b>	<b>12</b>
Alex-Cristian Constantin, Dragoș Tudorache, Adelin Japie, Cristina Alina Tătărău, Andrei Vlad Trăistaru, Vlad Constantin Zamfirescu, Radu Vlădăreanu	
<b>Caesarean section – morbidity and consequences .....</b>	<b>13</b>
Cezara Alina Dănilă, Ciprian Andrei Coroleucă, Cătălin Bogdan Coroleucă, Diana Comandașu, Mihai Mitran, Elvira Brătîlă	

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<b>The obstetrical impact of myomectomy .....</b>	<b>13</b>
Florina-Anita Dudău, A.F. Anca, Lucica-Elena Eddan-Vișan, Andreea-Elena Constantin, M. Ichim, Oana Mariana Murgeanu, Gina Ionescu-Anculete, Magdalena-Andra Bălan, Miruna Mînzală, Corina Grigoriu	
<b>The use of oxytocin in labor induction .....</b>	<b>14</b>
Mihai Cristian Dumitrașcu, Adina-Elena Nenciu, Cătălin Nenciu	
<b>Surgical management of infracentimetric breast cancer .....</b>	<b>14</b>
Alexandru Filipescu, Oana Solomon, Radu Vlădăreanu, Georgiana Bolocan, Andrei Trăistaru, Vlad Zamfirescu, Andreea Boiangiu	
<b>The impact of adipokines on fertility .....</b>	<b>15</b>
Elena Gheorghe, Cristiana Odukoya, Ioana Iordache, Elvira Brătilă, Andreea Carp Velișcu	
<b>Algorithm for the management of ovarian endometrioma .....</b>	<b>15</b>
Mihaela Grigore, Loredana Himiniuc	
<b>Challenges of a simple diagnosis in obstetrics and gynecology – bacterial vaginosis .....</b>	<b>16</b>
Corina Grigoriu	
<b>Short- and long-term hormonal stimulation side effects in infertile patients diagnosed subsequently with malignancy .....</b>	<b>16</b>
Andreea Hetea, Ruxandra Stănculescu, Anca Angela Simionescu	
<b>Ectopic pregnancy – current approach .....</b>	<b>17</b>
Andreea-Denisa Hodorog, Marina Dinu, Andreea Cismaru, Luciu Elinor, Ștefania Tudorache	
<b>News about anti-SARS-CoV-2 immunization .....</b>	<b>17</b>
Mihaela Ichim, Andreea Borisavlschi, Alina Marin, Ioana Gabriela Calo, Mihaela Boț, Aida Petca, Radu Vlădăreanu	
<b>Classic statistics versus artificial intelligence (AI) in estimating the birth outcome .....</b>	<b>18</b>
Dominic Iliescu, Laurențiu Dîră, Roxana Drăgușin, Smaranda Belciug	
<b>Intestinal occlusion by ileal endometriosis in a patient with chronic pelvic pain syndrome .....</b>	<b>18</b>
Gina Ionescu-Anculete, Adina Lungu, Corina Pârâu, Magdalena-Andra Bălan, Miruna Mînzală, Anita Florina Dudău, Oana Mariana Murgeanu, Alice Negru, Corina Grigoriu	
<b>Congenital hypofibrinogenemia in pregnancy – a case report .....</b>	<b>19</b>
Adelin Japie, Alex-Cristian Constantin, Dragoș Tudorache, Cristina Alina Tătăruș, Andrei Vlad Trăistaru, Vlad Constantin Zamfirescu, Radu Vlădăreanu	
<b>Immunological conflict in IVF .....</b>	<b>19</b>
Ioana Iordache, Cristiana Odukoya, Mihaela Braga, Alina Bordea, Andreea Carp Velișcu, Elvira Brătilă	
<b>Binder type nasomaxillary dysplasia – case report .....</b>	<b>20</b>
Alina-Gabriela Marin, Mihaela Boț, Mihaela Ichim, Andrei Cristian, Aida Petca	
<b>Adenomyosis: a challenge of diagnosis and therapy .....</b>	<b>20</b>
Claudiu Mărginean	
<b>Management of pregnant women with viral hepatitis B. The experience of the “Prof. Dr. Panait Sîrbu” Clinical Hospital of Obstetrics and Gynecology between 2019 and 2020 .....</b>	<b>21</b>
Mihai Mitran, Roberta Grațîela Deaconescu, Elvira Brătilă	
<b>Gynecological and women’s healthcare during the COVID-19 pandemic .....</b>	<b>21</b>
Mihai Mitran, Octavia Velicu, Elvira Brătilă	
<b>From asymptomatic bacteriuria to toxic septic shock in pregnancy .....</b>	<b>22</b>
Miruna-Oana Mînzală, Gina Ionescu-Anculete, Lucica Eddan-Vișan, Magdalena-Andra Bălan, Anita Florina Dudău, Oana Mariana Murgeanu, Corina Grigoriu	

<b>Parapagus dicephalus: prenatal diagnosis and assessment of associated malformations. Case report .....</b>	<b>22</b>
Alexandra Elena Munteanu, Mona Elena Constantin, Simona Vlădăreanu, Adriana Tecuci, Ciprian Pop-Began, Radu Vlădăreanu	
<b>Postpartum renal failure related to neglected systemic lupus erythematosus .....</b>	<b>23</b>
Mariana Oana Murgeanu, A. Badiu, Andra-Magdalena Bălan, Miruna Mînzală, Gina Ionescu-Anculete, Anita Florina Dudău, Corina Grigoriu	
<b>HPV diagnosis and biomarkers .....</b>	<b>23</b>
Șerban Năstăsia, Anca Popa, Anca Simionescu, Manuela Cristina Russu	
<b>Imagistic correlations between ultrasound and MRI examination of the fetus with congenital diaphragmatic hernia .....</b>	<b>24</b>
Erick Neșțianu, Cristina Guramba Brădeanu, Ioana Drăgan, Radu Vlădăreanu	
<b>Therapeutic approach to managing menopause .....</b>	<b>24</b>
Cristiana Odukoya, Ioana Iordache, Mihaela Braga, Elena Alina Bordea, Elvira Brătîlă, Andreea Carp Velișcu	
<b>Impact of COVID-19 on pregnancy services .....</b>	<b>25</b>
Dana Oprescu	
<b>News on HPV infection of uterine cervix .....</b>	<b>25</b>
Gheorghe Peltecu	
<b>Treatment and prophylaxis with tranexamic acid in obstetric hemorrhage .....</b>	<b>25</b>
Aida Petca, Andreea Borislavschi, Ioana Gabriela Calo, Mihaela Bicer, Ioan Teodor Bajeu, Mihaela Boț	
<b>New approaches to predicting and diagnosing preeclampsia – Congo red dot test paper .....</b>	<b>26</b>
Aida Petca, Mihaela Boț, Ioan Teodor Bajeu, Andreea Borislavschi, Ioana Calo, Mihaela Bicer, Mona Zvâncă	
<b>Acute respiratory distress syndrome (ARDS) in pregnancy caused by SARS-CoV-2 .....</b>	<b>26</b>
Liana Pleș, Georgiana Răducanu, Anca Daniela Stănescu, Romina-Marina Sima	
<b>COVID-19 vaccination in pregnancy and breastfeed period – pro and con arguments .....</b>	<b>27</b>
Liana Pleș, Tina-Ioana Bobei, Cristina-Diana Pomană, Romina-Marina Sima	
<b>Timing neuroprotection in perimenopause .....</b>	<b>27</b>
Manuela Russu	
<b>Caesarean section surgery in the 21<sup>st</sup> century .....</b>	<b>28</b>
Anca A. Simionescu	
<b>Update regarding breast cancer screening .....</b>	<b>28</b>
Oana Toader, Alexandra Olaru, Ramona Mircea-Vicol, Ramona Dragomir, Mădălina Mârza, Laura Ianculescu, Nicolae Suci	
<b>The road to ovarian cancer screening .....</b>	<b>29</b>
Dragoș Tudorache, Alex-Cristian Constantin, Adelin Japie, Cristina Alina Tătăruș, Andrei Vlad Trăistaru, Vlad Constantin Zamfirescu, Radu Vlădăreanu	
<b>Detailed genetic testing in fetuses with structural anomalies .....</b>	<b>29</b>
Mona Elena Zvâncă	

SUMMARIES OF 4<sup>TH</sup> EDITION OF PERINATOLOGIA.RO FORUM,  
BUCHAREST, ROMANIA, MARCH 25-27 2021

<b>Umbilical cord blood gas analysis – a valuable marker of perinatal hypoxia-ischemia .....</b>	<b>30</b>
Claudiu Angelescu, Daniela Eugenia Popescu, Ana Maria Cristina Maciu, Constantin Ilie	
<b>Immaturity of the digestive system of the premature baby – clinical and nutritional implications.</b>	
<b>Clinical case .....</b>	<b>30</b>
Anca Larisa Barac, Iustina Beşleagă, Anca Monica Şeicaru (Dumitrescu), Cristian Mihaï, Silvia Elena Ionescu, Simona Vlădăreanu	
<b>Fetal and neonatal alloimmune thrombocytopenia: early antenatal diagnosis leading to successful management after birth in the second pregnancy – case report .....</b>	<b>30</b>
Andreea Mădălina Bănică, Alexandra Popa, Ana Maria Predescu, Simona Daniela Popescu, Simona Vlădăreanu	
<b>Congenital hepatic vascular malformations: diagnostic and therapeutic aspects .....</b>	<b>31</b>
Ligia Blaga, Otilia Fufezan, Carmen Asăvoaie	
<b>Neonatal hypoxic-ischemic encephalopathy – specific lesions in the premature newborn .....</b>	<b>31</b>
M. Boia, D. Cioboată, F. Doandea, N. Lungu, T. Brandibur, A.I. Munteanu, A. Manea	
<b>Difficulties in the nutritional recovery of the newborn with digestive tract malformation .....</b>	<b>32</b>
Timea Brandibur, Maria Manea Aniko, Daniela Cioboată, Nicoleta Lungu, Florina Doandea, Mariana Boia	
<b>Autoimmune disorders in pregnancy and their impact on the neonate .....</b>	<b>32</b>
Cristina Buzduga, Arina Sirbu, Elena Szini, Laura Ştefan	
<b>Cerebral fetal destructive process – case presentation .....</b>	<b>33</b>
Cristina Chiriac, Adriana Dan	
<b>Newborn with hemolytic disease – hereditary etiology and case presentation .....</b>	<b>33</b>
Cristina Chiriac, Adriana Dan	
<b>Controlled hypothermia – the main neuroprotective strategy in newborns with moderate or severe perinatal hypoxia .....</b>	<b>34</b>
C. Cornevi, A.N. Luca, M.C. Parpalea, I.G. Petrescu, A. Tecuci, S. Vlădăreanu	
<b>Neonatal meningitis with <i>Candida albicans</i> in a premature baby .....</b>	<b>34</b>
Adriana Dan	
<b>Alternative strategies in the treatment of neonatal sepsis .....</b>	<b>35</b>
Adriana Dan	
<b>Respiratory distress syndrome (RDS) and cytomegalovirus (CMV) pneumonia in an ELBW premature baby .....</b>	<b>35</b>
Adriana Dan	
<b>Thrombocytopenia assesment in the neonate .....</b>	<b>36</b>
Irina Franciuc	
<b>Noninvasive versus invasive respiratory support in respiratory distress with surfactant deficiency .....</b>	<b>36</b>
Monica Hăşmăşanu, Melinda Matyas, Ligia Blaga, Georgiana Nemeti, Sorana Bolboacă, Gabriela Zaharie	
<b>Neurological complications in preterm infants .....</b>	<b>37</b>
Daniela Iacob, Alina Petric, Emil Radu Iacob, Ileana Enătescu, Mirabela Dima	
<b>Fetal heart analysis in the first trimester. New kid on the block .....</b>	<b>37</b>
Dominic Iliescu, Ciprian Pătru, Dan Ruican, Rodica Nagy, Ruxandra Stoean, Cătălin Stoean	

<b>Retinopathy of prematurity: the importance of screening .....</b>	<b>38</b>
Nicoleta Lungu, Daniela Popescu, Florina Stoica, Cristina Maciu, Florina Doandea, Aniko Manea, Daniela Cioboată, Timea Brandibur, Mărioara Boia	
<b>Semilobar holoprosencephaly – a rare pathology in the clinical practice .....</b>	<b>38</b>
Ana Maria Cristina Maciu, Aniko Manea, Nicoleta Lungu, Florina Doandea, Timea Brandibur, Daniela Eugenia Popescu, Mărioara Boia	
<b>Congenital diaphragmatic defects in neonates – diagnostic difficulty .....</b>	<b>39</b>
Cătălina Maravela, Antonia Stroescu, Simona Daniela Popescu, Simona Vlădăreanu	
<b>Impact of maternal inflammation on preterm newborns .....</b>	<b>39</b>
Melinda Matyas, Monica Hășmășanu, Ligia Blaga, Gabriela Zaharie	
<b>The clinical progression of a newborn from a mother with HBP and HIV-positive – case study .....</b>	<b>40</b>
Cătălina Andreea Mutuligă, Ana-Maria Iana, Ana-Maria Paula Fitărau, Simona Daniela Popescu, Simona Vlădăreanu	
<b>Diagnosis difficulties in a suspected case of Zellweger syndrome .....</b>	<b>40</b>
Alexandra Neamtu, Aniko Manea, Nicoleta Lungu, Timea Brandibur, Florina Doandea, Daniela Cioboată, Mărioara Boia	
<b>CMV transmission through breastfeeding .....</b>	<b>41</b>
Andreea Niculescu, Andreea Radu, Alexandra Virtejaru, Ana Predescu	
<b>Potential new predictive risk factors for retinopathy of prematurity – where are we now? .....</b>	<b>41</b>
Luminița Păduraru, Maura-Adelina Hîncu, Gabriela-Ildiko Zonda	
<b>Vertical transmission of SARS-CoV-2 and outcomes of neonates born to mothers with COVID-19 .....</b>	<b>42</b>
Daniela Eugenia Popescu, Nicoleta Lungu, Andreea Cioca, Maria Cezara Mureșan, Corina Cristea, Ana Maria Cristina Maciu, Constantin Ilie, Mărioara Boia	
<b>Can corticosteroid therapy influence the management and prognosis of intractable seizures in newborns in view of reducing inflammation and improving eurodevelopmental outcome? .....</b>	<b>42</b>
Simona Daniela Popescu, Antonia Stroescu, Andreea Bănică, Simona Vlădăreanu	
<b>Congenital rubella and syphilis coinfection .....</b>	<b>43</b>
Ana-Maria Roșoga, Adriana Dan	
<b>Particularities of the newborns with fetal growth restriction in neonatal intensive care units .....</b>	<b>43</b>
A. Tecuci, S. Vlădăreanu, A. Popa, A. Barac, A. Luca, A. Constantinescu, R. Șerban	
<b>Neonatal hepatitis associated with plurimalformative syndrome, ascites fluid and LLA suspicion .....</b>	<b>44</b>
Denisa-Mariana Vasile, Aniko Manea, Nicoleta Lungu, Timea Brandibur, Florina Doandea, Daniela Cioboată, Mărioara Boia	
<b>Postnatal management of the newborn with congenital diaphragmatic hernia .....</b>	<b>44</b>
Teodora-Aida Vasile, Ioana-Sonia Iordache, Simona Daniela Popescu, Simona Vlădăreanu	
<b>Prevention and treatment strategies in necrotizing enterocolitis .....</b>	<b>45</b>
Gabriela Corina Zaharie, Monica Hășmășanu, Lucia Ghirca, Blaga Ligia, Melinda Matyas	
<b>Congenital anomalies of the lower urinary tract .....</b>	<b>45</b>
Gabriela-Ildiko Zonda, Andrada-Lorena Gafton-Oghina, Luminița Păduraru	



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# HOT TOPICS IN PERINATOLOGY

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## COVID-19 in pregnancy: the endothelial cell as the target cell

Alexandru Florin Anca, Andreea Constantin, Corina Grigoriu, Anița Dudău, Lucica Vișan, Alexandru Badiu, Doru Câmpean

Bucharest University Emergency Hospital, Romania

SARS-CoV-2 continues to be a major problem for our health. And, unfortunately, there are many unanswered questions about the pathogenic mechanism. Among these, there is the one about the target cells once the virus invaded the body, because of the multiple manifestations: respiratory, nervous, digestive, cardiovascular etc. We think that we have some relevant information from the association between pregnancy and COVID-19. In many cases, the manifestations were similar to the ones from preeclampsia (when the infection was in the second half of the pregnancy). Or, if the patient already had preeclampsia, the manifestations worsened. It's now generally accepted

that the central pathogenic event in preeclampsia is the suffering of the endothelial cell. And hence the pathogenic well-known consequences, maternal and placental-fetal. This is why we can consider now that there is a third mechanism of aggressing the endothelium in pregnancy, besides the ones induced by the coagulation disorders and the diabetes. Thus, if we can consider the endothelial cell the target in the COVID-19, we have a reasonable explanation for the multitude of manifestations in this disease, including the vascular ones.

**Keywords:** COVID-19, endothelial cell, target cell, pregnancy, preeclampsia

## Current treatment options for women with pelvic organ prolapse

Diana Badiu, Vlad I. Tica

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Pelvic organ prolapse (POP) is caused by a weakening of the pelvic floor structure. The exact prevalence of POP is difficult to assess, and can be diagnosed based on the onset of symptoms. In this review, we describe the latest POP treatments, including pelvic floor muscle training, vaginal pessaries, vaginal apical suspension, transvaginal and sacrocolpopexy mesh. Knowing that the medical treatment cannot totally correct the pelvic floor herniation, this can help alleviate the major

symptoms. On the other hand, the disadvantage of the surgical intervention is represented by recurrence, but advanced surgical techniques have decreased the rate of recurrence. Therefore, POP treatment should be individualized for every woman, based on symptoms and comorbidities, taking also into account the woman's preference for a specific treatment.

**Keywords:** pelvic organ prolapse, treatment, apical suspension, sacrocolpopexy, transvaginal mesh

## Possible complications which can appear from using intrauterine devices

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**Introduction.** Intrauterine devices (IUD) are used for contraception or hormone replacement. The use of intrauterine devices may also be preceded by side effects, such as: cramps, IUD fragmentation, expulsion, infections, sepsis, vaginal insertion reaction. Serious complications, such as ectopic pregnancy or pelvic inflammatory disease, can occur in about 1% of cases. The most severe complication is uterine perforation, which can appear in 1 in 1000 cases. **Materials and method.** We present the case of a 42-year-old patient who came for pelvic pain. From the anamnesis, we found out that the patient was carrying an IUD (copper IUD) for 10 years, all this time not being investigated gynecologically. The IUD had been removed 14 days ago, without prior antibiotic treatment. The abdominal and pelvic CT revealed images suggestive of bilateral tubo-ovarian abscesses. At the time of hospitalization, the patient had a significant

clinical and biological inflammatory syndrome that improved under antibiotic, analgesic and antiinflammatory treatment. Two weeks after starting the treatment, the ultrasound showed a decrease in the size of the adnexal collections. **Discussion.** In addition to the contraceptive effect, wearing IUD comes also with many infectious risks, which patients neglect. The periodic gynecological evaluation for possible genital infections, as well as an appropriate antibiotic therapy at the time of insertion and removal of the IUD can reduce the complications. **Conclusions.** The delayed presentation to the emergency room, despite continuous severe pain symptoms, as well as the lack of the appropriate treatment at the time of IUD extraction led to a severe form of pelvic inflammatory disease, manifested by bilateral tubo-ovarian abscesses.

**Keywords:** IUD, pain, abscess



## Conservative management of caesarean scar pregnancy using uterine artery embolization

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Caesarean scar pregnancy (CSP) is an unwanted, extremely dangerous clinical pathology, a consequence of a previous caesarean delivery, which can lead to massive blood loss and even death in mothers due to increased depth of trophoblastic invasion. If left alone, CSP can result in miscarriage, heavy bleeding, rupture of the uterus, or abnormally invasive placenta, which in turn are causes of premature delivery, hysterectomy and multiple transfusions. Placentation anomalies are amongst the leading causes of maternal morbidity and mortality worldwide. To date, there is no international standard of the prediction of the extent of invasion and of the optimal management. Planned caesarean hysterectomy with the placenta left *in situ* was the gold standard for a long time. However, more than new 40 different methods of uterus sparing techniques have evolved in order to preserve fertility. The management

of CSP is also fraught with complications that can reach a 60% complication rate. Since there is no agreement upon treatment, every obstetrician and gynecologist manage the cases differently. There is an urgent need to develop treatment guidelines for CSP, in order to prevent accreta spectrum disorder and to decrease the risk of complications. We report a series of cases conservatively treated by uterine artery embolization generally offered after an injectable administration of one dose of methotrexate. The evacuator maneuvers following embolization are done 48 hours after the embolization, with minimum blood loss. We present the particularities of Doppler studies and the dynamics of hCG from our cases, which have been enrolled in the international registry of caesarean scar pregnancy.

**Keywords:** caesarean scar pregnancy, invasive placenta, uterine artery embolization

## Proposals for national improvement of screening and early diagnosis for genito-mammary malignancy

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We evaluated breast and cervical cancer-related deaths, age-standardized mortality rates and the contribution of breast and cervical cancers to life expectancy. Trends and percentage changes were compared between Romania and EU-27 for breast and cervical cancer, all cancer and all causes of mortality. We found a higher increase of breast and cervical cancer deaths in Romania. The health gap compared to EU is aggravated by the fact that no population screening for breast cancer is organized in the country and, unfortunately, cervical cancer screening is ineffective. The endometrial biopsy screening for the women with Lynch and Cowden syndromes is recommended starting from 35-40 years old, or five years earlier than the age of

diagnosis for the first endometrial cancer case in the family; for women in postmenopause, an annual transvaginal ultrasound is recommended. The dysfunctional cancer registry makes that screening to be absolutely inoperative. The opportunities for organizing these programs are consistent, but they should be increased in the future, in order to control the health gap between Romania and EU. More efforts and resources should be concentrated in the next years in order to ensure a universal access to breast and cervical cancer screening, and also for the early diagnosis of endometrial cancer for eligible women.

**Keywords:** breast cancer, cervical cancer, endometrial cancer, screening, national program

## Rare cases of maternal pathology associated with pregnancy

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We present five cases of maternal pathology associated with pregnancy, which request urgent clinical guidelines elaboration in order to improve maternal and fetal outcome. Human T-lymphotropic virus (HTLV) is considered to be the most highly oncogenic existing virus, being the cause of several fatal diseases. Specific information on prevention is lacking among the population and even among healthcare providers, especially in pregnancy associated with significant transmission, mostly by breastfeeding. *Polycythemia vera* is a rare chronic myeloproliferative neoplasm which represents an additional thrombotic factor in pregnancy. By identifying the women suffering from *polycythemia vera* and applying the latest standard in healthcare, including immunomodulatory and antiaggregant treatment, fetal and maternal prognoses are significantly improved. There are various causes for the late diagnosis of gastric cancer in pregnancy, nausea and vomiting being considered to be secondary to normal pregnancy and not further investigated, but endoscopy must be indicated in all cases of prolonged

symptoms and with weight loss more than 5%. *Pemphigoid gestationis* is a rare autoimmune bullous disease that occurs during the second or third trimester of pregnancy and may be associated with an increased risk of prematurity and small for gestational age due to mild placental failure. The biopsy of the lesion and serum antibodies against BP180 are sensitive and specific for the differential diagnosis with other dermatoses of pregnancy, a consequently proper monitoring and treatment decreasing the risk of maternal and fetal complications. Clinical fetal thyrotoxicosis is a rare disease, occurring in 1-5% of pregnancies with Grave's disease. The mortality in fetal thyrotoxicosis is 12-20%, mainly due to heart failure, but the assessment of TSH receptor stimulating autoantibodies, ultrasound fetal signs of hiperthyroidism and adequate antithyroid treatment may successfully guide the progression of pregnancy associated with Basedow's disease.

**Keywords:** human T-lymphotropic virus, pregnancy, *polycythemia vera*, gastric cancer, *pemphigoid gestationis*, fetal thyrotoxicosis

## Spontaneous rupture of the internal iliac artery after pelvic radiotherapy – case report

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Recent years have brought with them an increase in the incidence of neoplasms worldwide and the need for radiotherapy. Unfortunately, Romania occupies a leading place in Europe in terms of cervical cancer in women and especially in terms of diagnosing this condition in late stages, when adjuvant radiotherapy is required. Although radiotherapy improves the survival rate for malignancies, it also produces a series of short- and long-term complications. Radiation-induced arteriopathy is a well-known complication which usually arises chronically after radiotherapy. Radiation effects on the surrounding tumoral tissue are unspecific, and radiation tissue injuries may vary a lot. When radiation arthritis arises acutely, spontaneous rupture or, more

rarely, thrombosis of the involved vessel may occur. Spontaneous rupture can occur within 4 to 32 weeks of radiotherapy and is often presented in literature after radiotherapy for head and neck cancers. The spontaneous rupture of the internal iliac artery is extremely rare and life threatening. Iliac radiation arteritis may be accompanied by radiation-associated iliac vein disease and small vessel disease, being a complex disease and a diagnostic and therapeutic challenge. We present the case of a woman who underwent neoadjuvant radiotherapy for cervical cancer and who presented to the emergency room in hemorrhagic shock.

**Keywords:** radiotherapy, arteritis, hemorrhagic shock

## Progesterone priming in controlled ovarian stimulation

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In the field of human reproduction, progress and change arise from the constant desire of *in vitro* fertilization (IVF) specialists to improve pregnancy rate and live birth rate. Controlled ovarian stimulation is one of the main factors that influence the success rate. Numerous studies have shown that, beside age, the number of oocytes retrieved is directly proportional to the rate of blastocysts and pregnancy rate. The use of progesterone and

its derivatives to block the LH surge is a new approach to ovarian stimulation. The advantages and disadvantages of using progesterone priming will be the subject of this paper. Progesterone priming can be used as a first choice in fertility preservation, oocyte donation or in patients in whom the freeze-all strategy is required.

**Keywords:** progesterone priming, controlled ovarian stimulation, freeze-all strategy

## Benefits of alpha-lipoic acid in high-risk pregnancy

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Alpha-lipoic acid (ALA) is a natural molecule, necessary to the human body in many metabolic reactions. Because most of the time the endogenous ALA is not enough, an exogenous source must be provided from food and dietary supplements. Once absorbed, the ALA molecule is oxidized, transforming into its reduced form – dihydrolipoic acid (DHLA). ALA/DHLA are powerful redox compounds that affect the direct and indirect antioxidant, antiinflammatory and immunomodulatory activities. ALA/DHLA reduces the levels of proinflammatory cytokines (IL-1 $\beta$ , IL-6, IL-8, IL-17), while in the meantime increasing the secretion of antiinflammatory cytokines (IL-10). It decreases the secretion of

prostaglandin E2 and nitrogen oxide by inhibiting the cyclooxygenase (COX-2) and, therefore, reduces the risk of miscarriage in the first trimester of pregnancy. The administration of ALA, in the first trimester, in patients with abortive disease, has shown great potential in accelerating the resorption of subchorionic hematoma and decreasing the resulted abdominal pain. Administered alongside with magnesium, ALA can put a stop to premature contractions. The promising hypothesis of antioxidant supplementation could play an essential role in lowering the abortion rates and premature birth.

**Keywords:** alpha-lipoic acid, abortion, premature birth, antioxidant, immunomodulatory, cytokines

## A new approach to polycystic ovary syndrome

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Polycystic ovary syndrome (PCOS) is the most frequent endocrine disorder among women of reproductive age. There is a constant need of update in this field. PCOS has a detrimental impact on fertility and quality of life, with poor long-term outcomes (obesity, diabetes, endometrial cancer). The diagnosis and management aren't well standardized. There are many flaws regarding this pathology: the inaccurate term used *polycystic*, the out-of-date diagnosis criteria established almost 20 years ago, and the incomplete prevention of long-term effects. There is clear evidence that PCOS management needs

improvement. Medicine has evolved so much recently, and researchers are constantly searching for a better treatment and for new molecules. Despite this, the prognosis of PCOS patients hasn't improved significantly. They need a holistic approach, one that would include a different lifestyle, vitamins/probiotic supplementation and weight loss. These small changes can make a difference: improved life quality and pregnancy rate, along with better long-term outcomes.

**Keywords:** PCOS, infertility, life quality, update, lifestyle, diet, supplements

## The impact of the association of maternal HIV infection with IUGR and premature birth on the neonatal outcome – case presentation

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Maternal HIV infection can have two consequences on the fetus: maternal-fetal transmission of the infection and perinatal complications, such as increased risk of preterm birth and the restriction of intrauterine growth. The risk of mother-to-child transmission of HIV infection is almost negligible as long as its prevention protocols are applied. However, the incidence of severe adverse perinatal outcomes among HIV-infected pregnant women is still high due to the two fetal complications. Preterm birth and intrauterine growth restriction are described as having a major influence on neonatal mor-

tality and morbidity in this population. The relationship between the two and the intrauterine exposure to HIV and to antiretroviral treatment remains controversial and unresolved. For a better understanding of this relationship, several possible hypotheses have been formulated, that premature birth and IUGR may be a direct effect of the virus, may result from immunosuppression, infection-associated comorbidities or from factors that are not associated with HIV. The use of antiretroviral therapy has also been suggested as a possible risk factor.

**Keywords:** IUGR, HIV, premature birth, antiretroviral

## Stillbirth in COVID-19 confirmed pregnancies

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The infection with the new type of coronavirus (SARS-CoV-2) affected the prenatal management and surveillance of pregnancies worldwide. Although the knowledge gained from previous human coronavirus outbreaks suggests that pregnant women and their fetuses are particularly susceptible to poor outcomes, the data concerning this type of infection during pregnancy are still limited somehow. There are few studies about the impact of maternal SARS-CoV-2 infection and the risk of vertical transmission. While most diagnostic tests performed in infants born to infected mothers have been negative, the virus has been identified in the placenta and the amniotic fluid, even though the new-

borns had no clear evidence of infection. The effects of vertical transmission of SARS-CoV-2 remain largely unknown. Some case reports confirmed stillbirth associated with transplacental transmission with placenta and umbilical cord blood tested positive for the virus by PCR. Tissue samples from placenta revealed accelerated villous maturation, arterial thrombosis associated with decidual infarction, and inflammatory infiltrate. The microscopic evaluation of placenta and fetus can help elucidate the pathophysiology of COVID-19 in pregnancy.

**Keywords:** COVID-19, pregnancy, stillbirth, SARS-CoV-2, vertical transmission

## Caesarean section – morbidity and consequences

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Nowadays, the number of deliveries through caesarean section has significantly increased, along with the number of postoperative complications. When the medical situation justifies it, caesarean section can be a life-saving intervention, but this procedure can also lead to short-term and long-term health effects for women. Late postoperative complications can be divided into two main groups: obstetrical and gynecological complications. Gynecological complications include intraabdominal adhesions, endometriosis of the abdominal wall in the surgical scar, isthmocele and uterine prolapse. In some cases, the long-term morbidity determined by intraabdominal adhesions can cause chronic pelvic pain, intestinal obstruction or infertility. The caesarean scar defect, also known as isthmocele, is considered the main risk factor for low placenta insertion in subsequent pregnancies. Abdominal wall endometriosis has a low incidence, and it is due to iatrogenic seeding of endometrial cells during hysterotomy that create

a functioning endometrial tissue mass outside the uterine cavity. The obstetrical complications in future pregnancies include low placental insertion, placenta accreta, infertility or caesarean scar ectopic pregnancy. Morbidly adherent placenta (accreta, increta and percreta) is the abnormal placental invasion of the uterine wall, inducing failure of placental separation at delivery. Caesarean scar ectopic pregnancy represents the implantation of the embryo in the caesarean scar and it is a rare form of ectopic pregnancy that can lead to severe complications such as uterine rupture and haemorrhage. Any process that disrupts or scars the endometrium and myometrium can result in abnormal pregnancy implantation. Due to the rising rate of caesarean deliveries in recent years, it is important for clinicians to be aware of the complications associated with this procedure.

**Keywords:** caesarean delivery, isthmocele, adhesions, abdominal wall endometriosis, morbidly adherent placenta, caesarean scar ectopic pregnancy, infertility

## The obstetrical impact of myomectomy

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**Introduction.** The risk of uterine rupture in a pregnancy, after laparotomy or laparoscopic myomectomies, is low. There are studies that reveal an incidence of 4 cases after laparotomy and 10 cases after laparoscopy, out of 1000 patients. Both abnormal adherent placenta and uterine rupture in a single patient are rare. **Case report.** We describe a case of uterine rupture after three years after a laparotomy myomectomy was practiced. A 32-year-old patient, at the first pregnancy, within the 22<sup>nd</sup> week of gestation, with a placenta praevia and a suspicion of abnormal adhesion, showed up at the emergency room for a psycholeptic episode, where free intraperitoneal fluid was discovered on ultrasound. An exploratory laparotomy was practiced which found a high quantity of blood clots and a uterine hole at the level of the uterine fundus through which the amniotic sac could be seen. The fetus was extracted, but the placenta was only partially removed due to bleeding.

A total hysterectomy with bilateral salpingectomy for the abnormal adherent placenta accreta was performed.

**Discussion.** The anatomopathological result sustained the diagnosis of abnormal adherent placenta increta and of uterine rupture. Usually, the uterine rupture appears in the third trimester of gestation or during labor. The number of cases in the second trimester is low and is often found after recent surgery. **Conclusions.** Even though the risk of uterine rupture is under 1%, the cases which need a surgical intervention for myomectomy must be chosen carefully. It seems that the risk of uterine rupture after caesarean section is higher than after myomectomies performed through laparotomy or laparoscopy. The operative technique is an important element – the involvement of the endometrial cavity, the number of scar tissue zones or hysterorrhaphy in two layers.

**Keywords:** myomectomy, uterine rupture, laparotomy

## The use of oxytocin in labor induction

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Labor induction is a common procedure, usually used when the benefits of this procedure exceed the expectative approach. The use of exogenous oxytocin for the onset and augmentation of labor has increased in recent years. Multicenter studies, with large groups, analyzed the benefits of labor induction at 39-40 weeks compared to spontaneous labor onset after this period. The potential adverse reactions to oxytocin led to reevaluations of current practice guidelines. Currently, one can choose to induce labor in case of the need to speed up childbirth, reduce the duration of labor, maternal pathologies, and

even to reduce the risk of caesarean section. The choice of labor should be evaluated for each patient, taking into account the indications and contraindications. The medical team should rigorously inform the patient regarding the risks and benefits. The informed consent should be signed. In this paper, we present the currently recommended protocols for labor induction, induction of labor at the reception at 39 weeks, and about use of oxytocin in these cases.

**Keywords:** oxytocin, labor induction, pregnancy at term, expectative management in pregnancy

## Surgical management of infracentimetric breast cancer

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Breast cancer is the most common malignancy in female patients worldwide. As a result of the well-developed screening programs, half of non-metastatic breast cancers are now diagnosed at an infracentimetric stage. Surgery remains the first-line treatment for breast cancer, with many early-stage patients being cured with surgery alone. The surgical treatment of breast cancer has evolved significantly in recent years, the conservative treatment being the first option for many surgeons and their patients. The goals of breast-conserving cancer surgery include the complete resection of the infracentimetric primary tumor, with negative margins to reduce the risk of local recurrences – ideally, a 1 cm margin

around lesion, but leaving as much normal breast tissue as possible, and the resection of the axillary lymph nodes to provide necessary prognostic information. Sentinel node biopsy is considered an alternative to standard axillary node dissection, but it is not an option for patients with enlarged level I and level II lymph nodes. The options for axillary lymphadenectomy are: complete axillary node dissection, axillary dissection of levels I and II lymph nodes, sentinel lymph-node biopsy. Conservative surgery of infracentimetric breast cancer is followed by a course of breast radiation therapy in order to reduce the risk of cancer recurring in the breast in the future.

**Keywords:** conservative, breast, lymphadenectomy

## The impact of adipokines on fertility

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Along with hypertension, dyslipidemia and insulin resistance, obesity belongs to a cluster of endocrine disturbances identified as the "metabolic syndrome". A significant proportion of the infertile or subfertile populations are obese or overweight. Fatness has a negative influence upon a woman's frequency of ovulation, leading to infertility and also to increased rates of miscarriage. Furthermore, in later pregnancy, it can be the source of severe complications for both mother and child. Many studies concluded that the risk of infertility for obese women is three times higher than for the non-obese patients. Weight loss has been associated with a significant rise of ovulation and, moreover, with an increase of the pregnancy rate and pregnancy outcome. Adipose tissue functions as a highly specialized endocrine and paracrine organ, producing an array of adipokines, as well as eliciting cell-mediated effects *via* proinflammatory and antiinflammatory cells, generating various cytokines and chemokines. These factors have local and systemic biological effects, influencing insulin sensitivity. Alterations in adipokine levels or in their mechanism of action are associated with fertility

impairment and pregnancy complications, as well as with obesity, metabolic syndrome and cardiovascular diseases. Normal levels of adipokines, such as leptin, adiponectin, resistin, omentin and chemerin, are fundamental to maintain the integrity of the hypothalamus-pituitary-gonadal (HPG) axis, regular ovulatory processes, successful embryo implantation, and physiologic pregnancy. Nevertheless, the expression of insulin-sensitizing adipokines varies with adipose tissue abundance. These adipokines have demonstrated both the potential effects on ovarian function and the possible effects on the formation of the placenta, acting through multiple mechanisms. In the past years, new directions are emerging in the field of fertility and reproduction, regarding the integral role of adipokines in the normal physiology of the reproductive system with complex interactions at all levels of the HPG axis. Observational studies have demonstrated that states of their excess, deficiency or resistance can be associated with abnormal reproductive function.

**Keywords:** adipokines, obesity, infertility, metabolic syndrome, adipose tissue

## Algorithm for the management of ovarian endometrioma

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Ovarian endometriomas represent the most common form of endometriosis. In literature, there is much debate regarding the management of these cysts in infertile women, particularly before the use of assisted reproductive technologies. Some pieces of evidence support the surgical excision of ovarian endometriomas, while others recommend with caution the surgical intervention. In order to apply a correct management, certain factors need to be analyzed: the patient's symptoms, age, ovarian reserve, size and laterality of the cyst, prior surgical treatment, and the level of suspicion for malignancy. Recent data from literature suggest that certain patients' profiles may benefit from proceeding directly to *in vitro* fertilization (IVF). In this

group, there are included: older patients, those who have diminished ovarian reserve, those who have bilateral endometriomas, or those who had a prior surgical treatment. Although endometriomas can be detrimental to the ovarian reserve, the surgical therapy may further lower a woman's ovarian reserve. Regardless of treatment plan, infertile patients with endometriomas must be counseled appropriately before choosing either treatment path. This paper presents an algorithm for the management of ovarian endometrioma, taking into account factors such as size, age of the patient, symptoms and infertility.

**Keywords:** ovarian endometrioma, management, endometriosis, *in vitro* fertilization

## Challenges of a simple diagnosis in obstetrics and gynecology – bacterial vaginosis

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**Introduction.** Bacterial vaginosis is characterized by a complex imbalance of the vaginal flora. Doderlein lactobacilli are replaced by anaerobic germs (*Gardnerella vaginalis*, *Prevotella* spp., *Porphyromonas* spp., *Bacteroides* spp., *Mobiluncus*, *Megashpera*, *Sneathia*, *Clostridiales* spp. etc.). It is frequently underdiagnosed, especially because many patients are asymptomatic, although they have recognition criteria. **Discussion.** The implications of bacterial vaginosis are important, beyond the patient’s subjective discomfort. Thus, in obstetrics, bacterial vaginosis can be involved in the increased risk of miscarriage, premature birth, amniotic infection, premature rupture of membranes and postpartum endometritis, regardless of delivery type. There are discussions that show

frequent bacterial associations (mycoplasmas – anaerobic germs – bacterial vaginosis). Also, in nonpregnant patients, associations of vaginosis with cervicitis, endometritis, pelvic inflammatory disease, complications of IUDs and cellulitis of the vaginal cuff after hysterectomy can be found more frequently. A peculiarity of vaginosis is the frequent recurrence rate, which confuses both the patient and the therapist. **Conclusions.** With these arguments, we advocate a correct, proactive diagnosis in patients at risk, with a correct conduct both in terms of the chosen drugs, and especially for the prevention of recurrences.

**Keywords:** bacterial vaginosis, diagnosis, treatment, complications

## Short- and long-term hormonal stimulation side effects in infertile patients diagnosed subsequently with malignancy

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**Introduction.** There is a global increase in infertile couples, due to both female and male causes. Approximately 19% of Romania’s population faces infertility, therefore couples decide for fertility medical treatments. There have been many debates regarding the association between infertility drugs and cancer. Since these drugs have consequences on steroidogenesis, they can lead to various types of cancer, including breast, ovarian or endometrial cancer. Hormonal regimens used to increase the number of follicles and oocyte maturation lead to an increased serum level of estrogens, higher than a regular menstrual cycle. These estrogens can lead to an increased risk of estrogen-dependent tumors. Repeated ovulation induced through ovarian hyperstimulation modify the natural ovarian cycle and ovarian epithelium leading to ovarian epithelium’s malign transformation. We have to take into consideration that some cancers are hormonal dependent. Therefore, there is a physiologic mechanism between drug stimulation and an increased risk of cancer development. Moreover, the women’s age at the stimulation onset is also associated with an increased risk of cancer. **Materials and method.** The purpose of this presentation is to analyze if there is an association between medications used for fertility treatments and

cancer, based on articles published on Web of Science Core Collection, PubMed, Scopus and Medline, using the keywords: “hormonal stimulation”, “cancer”, “fertility”, “infertility”, “treatment”. Results. The medical data that analyze the relationship between fertility drugs and cancer are scarce; there are mainly observational studies. Recent studies state that there is no definitive relationship between fertility drugs and cancer, and some authors concluded that estrogen protects against colorectal cancer. High doses of clomiphene (2000 g, with the initial dose of 50 g) used for seven or more cycles increase the risk of cancer. **Discussion.** Due to an increase use of fertility treatments and to an increase in gynecological cancer incidence in women of fertile age (especially ovarian cancer), ovarian stimulation must be used with precaution. Patients who decide on *in vitro* fertilization should be informed regarding the future consequences; moreover, a national register of these patients should be taken into consideration. **Conclusions.** Before fertility treatment, doctors should evaluate the patients, including the risk factors for cancer. When going for reproductive medical therapies, personalized treatments should be mandatory.

**Keywords:** cancer, fertility treatment, ovarian stimulation, *in vitro* fertilization



## Ectopic pregnancy – current approach

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**Introduction.** Ectopic pregnancy (EP) remains an important health problem. It affects fertility and has significant costs. The optimal management in both tubal (salpingectomy or salpingostomy) and non-tubal (especially in rare locations) is still unclear. We aimed to review the recent literature and to present our experience during two years. **Materials and method.** We searched PubMed for studies published in English on EP in the last five years. Manuscripts using Consolidated Standards of Reporting Trials (CONSORT) guidelines and checklists for usefulness of research were elected. Also, all files of patients admitted in our teaching hospital with the suspected diagnosis of EP (from January 2020 to December 2021) were included. Data were collected retrospectively. Main outcome measures were: age, parity, implantation site, presentation, the main risk factor(s), the diagnosis-intervention interval, and the management applied. **Results.** Articles from selected high-impact journals were thoroughly studied. We noted an increase in systematic reviews, meta-analyses and case reports. High-quality randomized control trials (RCTs) were scarce. Very few addressed

important clinical questions and fewer have results with a potential to change the standard care. In our hospital, 151 EP cases were managed during the study period. The majority of them were tubal and managed with emergency abdominal salpingectomy. The number of laparoscopic interventions for EP decreased dramatically in 2020. We encountered rare cases: third-trimester abdominal EP, ectopic interstitial molar pregnancy, chronic EP, cervical ectopic pregnancy. The incidence of caesarean scar pregnancy (CSP) increased, and all cases were managed by abdominal emergency hysterectomy. **Discussion.** In recent years, the number of articles on EP has remained stable and the number of meta-analyses increased. There was a decrease in the number of published RCTs. We should share the experience and improve our research practices. **Conclusions.** In our studied population, EP remained life-threatening at times. We should struggle to preserve the fertility in all remaining cases, despite limitations imposed by SARS-CoV-2 pandemic.

**Keywords:** ectopic pregnancy, caesarean scar ectopy, laparoscopy, laparotomy, emergency

## News about anti-SARS-CoV-2 immunization

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The new type of coronavirus (SARS-CoV-2) is an enveloped positive-sense single-stranded RNA virus which causes the coronavirus disease 2019 (COVID-19). In most cases (>90%), the patients are asymptomatic or develop mild symptoms. The impact of this virus continues to overwhelm the healthcare systems, therefore, starting with 1 December 2020, the U.S. Food and Drug Administration has approved two types of vaccines, based on phase 3 clinical trial efficiency data: Pfizer and Moderna vaccines use messenger RNA-based technology, with 95% and 94.1% efficacy, respectively, while AstraZeneca has developed a viral vector-based vaccine. Since the immune response to vaccination in pregnant women cannot be assumed from that of the

general population, and because the assessment of safety of vaccination in pregnancy is unique, pregnant women were excluded from phase 3 clinical trials. The availability of vaccine efficacy and safety data during pregnancy is thus limited, thereby the decision to vaccinate pregnant women remains between the patient and obstetrician, to weigh the risks and benefits. The Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the American Society for Maternal-Fetal Medicine have issued recommendations in support of COVID-19 vaccination of pregnant women.

**Keywords:** pandemic, vaccination, coronavirus, pregnancy

## Classic statistics versus artificial intelligence (AI) in estimating the birth outcome

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**Introduction.** In the last decade, the use of neural computing for automatic differential diagnosis has rapidly spread. Neural networks, being able to learn from labeled input data, are flexible and powerful when applied to medical diagnosis. **Objective.** One of the goals of modern obstetrics is the prediction of the delivery mode, preferable before the onset of labor, as the emergency operative delivery is associated with high fetal and maternal morbidity and mortality. The aim of this observational study was to determine by classic biostatistics and neural computing means if the clinical and ultrasound weekly evaluation at term in nulliparous women may serve for the prediction of labor outcome. **Materials and method.** Clinical and ultrasound weekly evaluation were performed at term using a combination of parameters previously proposed

in literature for labor outcome: fetal head engagement (head to perineum distance, progression distance, angle of progression), occiput position, estimated fetal weight, cervical length, Bishop score. **Results.** The classic statistics could not provide significant correlations of the measured parameters and the delivery mode. Using artificial intelligence (AI), the chosen variables are indeed strongly and significantly correlated with the delivery mode, and the chosen technique appears appropriate for solving this real-life problem. **Conclusions.** AI performs better than classic statistics in estimating labor outcome, and certain algorithms may serve in the future for labor counseling.

**Keywords:** transperineal ultrasound, birth, artificial intelligence, delivery mode, vaginal birth, caesarean delivery, head station, occiput position

## Intestinal occlusion by ileal endometriosis in a patient with chronic pelvic pain syndrome

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**Introduction.** The gastrointestinal tract is the most common site of extrapelvic endometriosis, affecting 5-15% of women with pelvic endometriosis. Terminal ileum is rarely involved in endometriosis. Similarly, bowel endometriosis is an uncommon cause of intestinal obstruction. The treatment of endometriosis is medical and/or surgical. It is justified by the progression of the disease in most cases and by the impossibility of anticipating which of the cases will progress. **Materials and method.** We present the case of a 38-year-old patient with a history of chronic pelvic pain syndrome, dysmenorrhea and infertility, who came for abdominal-pelvic pain, total lack of intestinal transit of about 15 hours and vomiting. The abdominal and pelvic CT examination revealed a nodular formation on the right uterine adnexal which was about 50 mm that had intimate contact with the last ileal loop, associating at this level a sudden decalibration, and the upstream distension

of the other loops. The surgery was performed and a straight ovarian cystic formation with about 50 mm was found in the abdominal cavity, intimately adherent to the uterus and the last ileal loop, three fibrous stenoses at the level of the terminal ileum, the distal one being quasi-complete, the uterus being set in inside the pelvis by the adhesions. Straight annexectomy and segmental enterectomy were performed. The histopathological examination revealed right intestinal and adnexal endometriosis. **Discussion.** The early diagnosis and treatment in the early stages of endometriosis would have prevented the progression of the disease to the severe form that included the ileum. **Conclusions.** The patient came with acute surgical abdomen and intestinal occlusion, whose diagnoses did not necessarily indicate the suspicion of endometriosis. The patient was diagnosed belatedly with a severe form of endometriosis.

**Keywords:** ileal endometriosis, occlusion, pain

## Congenital hypofibrinogenemia in pregnancy – a case report

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Congenital hypofibrinogenemia is a rare bleeding disorder, defined by plasmafibrinogen levels below 150 mg/dl, frequently associated with a functional anomaly of fibrinogen (dysfibrinogenemia). The prevalence of this disorder is difficult to establish, due to the large number of asymptomatic cases, sometimes bleeding symptoms appearing only in certain situations, such as pregnancy. We report the case of a 39-year-old pregnant woman with congenital hypofibrinogenemia and high risk of spontaneous abortion due to cervical insufficiency. During investigations, we analyzed the variation of the plasma fibrinogen level from the moment of diagnosis

until now, and we tried to correlate the lowest levels with the symptoms. In the presented case, several replacement therapy sessions were required, the mainstay of treatment of bleeding episodes in these patients being plasma-derived fibrinogen concentrate. Cryoprecipitate and fresh frozen plasma are alternative treatments that should be used only when fibrinogen concentrate is not available. Even though the need for replacement therapy did not change during pregnancy, its availability before parturition is mandatory to prevent heavy bleeding.

**Keywords:** hypofibrinogenemia, pregnancy, replacement therapy, bleeding symptoms

## Immunological conflict in IVF

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The immune system plays a role in embryo implantation, as well as in the further development of pregnancy. Until recently, the entire literature was dedicated to peripheral blood natural killer cells (pbNK), but evidence has provided new insight into uterine natural killer cells (uNK). The fetus can express paternal antigens. Maternal immune system recognizes these structures as non-self, which can lead to rejection – immunological conflict. If donor oocytes are used, a higher number of non-self antigens are presented to the maternal NK cells,

compared to what happens in natural pregnancies. uNK cells have on their surface killer cell immunoglobulin-like receptors (KIRs), that bind to human leukocyte antigen (HLA-C). Immunologically, trophoblast invasion is one of the most critical moments of pregnancy. Some associations between KIR/HLA-C leads to recurrent implantation failure, recurrent miscarriage, foetal growth restriction or preeclampsia.

**Keywords:** immunological conflict, KIR, antigens, recurrent miscarriage

## Binder type nasomaxillary dysplasia – case report

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Binder type maxillonasal dysplasia – also known as Binder syndrome or nasomaxillary hypoplasia – is a rare congenital disorder, described first in 1882, that affects males and females in equal numbers. The incidence of Binder syndrome is less than 1 per 10,000 live births. The majority of cases occur sporadically, but there have also been reported familial cases. It is characterized primarily by a hypoplastic midface syndrome – a specific developmental anomaly that affects the anterior part of the maxilla and the nasal complex – and it consists of a spectrum of inadequate nasomaxillary osteocartilaginous framework, deficient nasal soft tissues and a short columella, therefore entailing a distinctive appearance to the individual facial structure as years pass by. Similar facial features have been seen in conditions such

as warfarin embryopathy, acrodysostosis and Stickler's syndrome, anomalies that must be taken into account for the differential diagnosis. The surgical correction of these facial anomalies and consequent orthodontic treatment can be laborious in order to achieve an adequate facial profile and their results might be disappointing regarding tissue expansion, associating unpredictable growth and resorption of the bone grafts in children. Despite the typical skeletal defects, Binder syndrome may also associate bilateral loss of hearing and various degrees of neurodevelopmental retard. We present a clinical case diagnosed within our clinic and the management we considered for this particular anomaly.

**Keywords:** maxillary underdevelopment, short nose, mental retardation

## Adenomyosis: a challenge of diagnosis and therapy

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Adenomyosis is a particular form of endometriosis, an insufficiently diagnosed condition and without a therapeutic standard. Its incidence among women of reproductive age is not yet known. About 30% of hysterectomy specimens have a histological diagnosis of adenomyosis. This microscopic finding is commonly associated with uterine fibromatosis and endometriosis. Several theories have emerged regarding the etiology of the disease, adenomyosis possibly having a traumatic, immunological, hormonal, metaplastic and stem cellular background. The incriminated risk factors are: parity, age, uterine scars, ectopic pregnancy, smoking, use of antidepressants and tamoxifen. Given the complications that adenomyosis carries upon, such as infertility, premature birth, uterine rupture and postpartum uterine atonia, its diagnosis should be established at an early age. The clinical evaluation, the transvaginal ultrasound with color Doppler and sonoelastography are usually part of this process. In certain situations, MRI is necessary for an appropriate

diagnosis. The ultrasound signs of adenomyosis are subtle and are represented by: increase in uterine volume, poorly defined transition zone, subendometrial cysts, "fan shaped shadowing", translesional color Doppler flow and increased rigidity upon sonoelastography. The hysteroscopic and laparoscopic evaluation indicates cystic and hemorrhagic lesions. There is no gold standard in terms of therapeutic approach, the treatment options being dependent on family planning. The medical options are represented by hormonal therapy. The surgical therapy consists of hysterectomy and hysteroscopic, laparoscopic or laparotomy excision of lesions. Alternative proposed therapies include high-intensity focused ultrasound, transcervical radiofrequency ablation and uterine artery embolization. In conclusion, the diagnosis of adenomyosis consists of clinical and ultrasound combination, but a consensus is needed for therapy, especially for infertile patients.

**Keywords:** adenomyosis, diagnosis, therapy

## Management of pregnant women with viral hepatitis B. The experience of the “Prof. Dr. Panait Sîrbu” Clinical Hospital of Obstetrics and Gynecology between 2019 and 2020

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Chronic hepatitis B virus (HBV) infection affects about 350 million individuals worldwide, with half of them acquiring the infection either perinatally, or in early childhood, especially in endemic areas. The management of HBV infection during pregnancy remains a challenge and involves various aspects of maternal and fetal care. The aim of this review is to present the current knowledge regarding pregnancy and HBV infection, as well as recent efforts to reduce the rate of mother-to-child transmission. We present the clinical experience with HVB-positive patients in the “Panait Sîrbu” Clinical Hospital of Obstetrics and Gynecology, between 2019 and 2020. We analyzed data from 47 HBV-positive pregnancies (41 patients with chronic HVB infection and six patients with HIV and HVB infections), resulting in 48 live childbirths. In our study group, the mean maternal age was 31±7 years old, and the majority were primiparous. Caesarean section was the birth method in 41 (87.24%) of the cases, with 43 (91.48%) being born at term. In seven cases (14.89%), spontaneous membrane rupture occurred. All the newborns received active immunoprophylaxis (HVB vaccine) and passive

immunoprophylaxis consisting in the administration of the hepatitis B immunoglobulin (HBIG). Although in most cases, acute or chronic HBV infection in pregnancy is similar to that in the general adult population, the testing for HVB is recommended in every pregnancy, regardless of the previous testing or vaccination, due to the higher incidence of low birth weight, prematurity, as well as gestational diabetes mellitus and antepartum hemorrhage reported in pregnancies with chronic maternal HBV infection. The identification of HVB-positive pregnant women remains the most effective way to prevent the HVB transmission to newborns, combined with passive and active prophylaxis at birth. Breastfeeding is not contraindicated for HVB patients, but is not recommended for women who take antiviral drugs, due to the potential teratogenic effect on the fetus. Finally, there remains no clear evidence that elective caesarean section reduces the risk of mother-to-child transmission compared to vaginal delivery.

**Keywords:** hepatitis B, pregnancy, MTCT, immunoprophylaxis

## Gynecological and women’s healthcare during the COVID-19 pandemic

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The COVID-19 pandemic has been straining healthcare systems globally, for over a year, with wide-reaching implications for health. Women experience unique health risks and outcomes, influenced by their gender – mainly, referring to the obstetrical and gynecological pathology. The present paper aims to address the main guidelines and suggestions for gynecological pathologies during the COVID-19 pandemic. We present the role

of telemedicine and of thoroughly triage of patients. While an in-person visit and physical exam cannot be fully replaced, telemedicine can provide a safer option for patients during the COVID-19 pandemic or for those who are quarantined and have no access to care. When possible, patients should be seen in person for confirmatory physical exams.

**Keywords:** COVID-19, gynecology, telemedicine

## From asymptomatic bacteriuria to toxic septic shock in pregnancy

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**Introduction.** Asymptomatic bacteriuria is found in about 9% of cases during pregnancy. It can progress to an upper urinary tract infection, causing multiple complications, gradually leading to sepsis or multiple organ failure. Sepsis in pregnancy is a particular situation, because the physiological changes can affect the immune system, producing a weaker response of the body to various infectious factors, even favoring certain types of infections. **Case presentation.** We present the case of a 16-year-old patient, known to be 23 weeks pregnant, in evolution. In the patient's medical history, we identified a positive urine culture for *Klebsiella*, three weeks before. The patient was admitted to the intensive care unit, with a severe general condition, with clinical and paraclinical inflammatory syndrome, hypotension and impairment of renal and hepatic functions.

Vasopressor, antibiotic and antiinflammatory support treatment was instituted to support the renal function, under which the evolution was favorable. **Discussion.** The case evolved from a benign and relatively common pathology, especially in pregnant women, asymptomatic bacteriuria, to an upper urinary tract infection, then sepsis and, in the end, to multiple organ failure, a situation of high severity and with an increased mortality rate. **Conclusions.** The case follows the evolution of a patient with improperly treated asymptomatic bacteriuria and its complications. It is very important to screen for asymptomatic bacteriuria, throughout the pregnancy, which, when ignored, can cause multiple damages to organs and systems, even leading to organ failure or death.

**Keywords:** bacteriuria, sepsis, pregnancy

## Parapagus dicephalus: prenatal diagnosis and assessment of associated malformations. Case report

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The incidence of multiple pregnancies has increased over the years, due to the improvement of reproductive techniques, and it's usually a reason to rejoice for the parents, although, from a medical point of view, it is considered a high-risk pregnancy. One of the strangest and rare complications is that of conjoined twins. The clinical diagnosis of conjoined twins is close to impossible; the use of auscultation or palpation can only suggest separate twins, and in places where access to basic technology is limited, the diagnosis can only be

confirmed at birth. The advances in ultrasonography allow the early depiction and a proper prenatal evaluation of this condition, better counseling for parents, including the termination of pregnancy and, if the pregnancy continues, establishing a plan of delivery in a specialized center, improving the chances to survive, and accomplishing the medical aim to surgically separate the twins.

**Keywords:** conjoined twins, *parapagus dicephalus*, twin monozygous pregnancy, surgical separation

## Postpartum renal failure related to neglected systemic lupus erythematosus

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**Introduction.** Systemic lupus erythematosus (SLE) is an autoimmune disease that affects women of reproductive age. Renal involvement, presented as a form of active lupus nephritis, during pregnancy or in the moment of conception, increases the risks of premature birth, intrauterine growth restriction, preeclampsia, maternal mortality and fetal death. Furthermore, the current guidelines advise that women with SLE should obtain a stable remission for at least six months before conception. The hormonal and immune changes during pregnancy can alter the activity and progression of the disease, the database suggesting a high risk of lupus nephritis during pregnancy. **Materials and method.** A 20-year-old woman (gravida 3, para 2), at 31 weeks of gestation, was admitted to our department, transferred from another hospital immediately after caesarean section, with severe preeclampsia and neglected systemic lupus erythematosus. At the admission to the intensive care unit, the patient had acute kidney failure (urea 173 mg/dl [normal values: 19.26-49.22 mg/dl], creatinine 9 mg/dl [normal values 0.7-1.3 mg/dl] and diuresis 300 ml per day), hypertension (her arterial blood pressure was 180/100 mmHg), and severe anemia (hematocrit

22.5% [normal values: 31.2-41.9%] and hemoglobin 6 g/dl [normal values: 10.9-14.3 g/dl]). Therefore, she was referred for nephrological assessment. The nephrologists put her on hemodialysis, corticosteroids (prednisone starting from 60 mg per day, gradually lowering the dose), anticoagulants (clexane, 0.4 ml two times daily), antihypertensives (Dopegyt®, Norvasc®, clonidine), and treatment for hematological recovery (2 units of RBCs and erythropoietin). Consequently, she was discharged from the hospital after thirty days, with a partial remission of kidney function (urea 74 mg/dl, creatinine 4 mg/dl and diuresis 700 ml per day) and of the hematological parameters (hemoglobin 8 g/dl). **Discussion.** Pregnant women with SLE should be under the care of a multidisciplinary team, consisting of a rheumatologist, a nephrologist and an obstetrician, considering the possible complications that can occur. **Conclusions.** As a result, these patients require a high grade of clinical suspicion and constant awareness by doctors, in order to minimize the burden of lupus nephritis.

**Keywords:** systemic lupus erythematosus, renal, pregnancy

## HPV diagnosis and biomarkers

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Although cervical cytology served as main cervical cancer screening tool, the low sensibility and the high percentage of unsatisfactory result of the test led to the development of new biomarkers for the primary screening or triage of positive screening results. The use of HPV DNA tests is the most important change in cervical screening strategies, either as routine primary screening tool, or as a triage tool for modified cytological screening results. Simultaneous dual staining of the p16INK4a proapoptotic and Ki-67 proliferative proteins is suitable for triaging women referred for abnormal cytology and could be a predictor of CIN2+ lesions. High levels of HPV messenger RNA for E6/E7 reveal overexpression of E6/E7 oncogenes, an event

associated with progression to cervical intraepithelial neoplasia and invasive cervical cancer. HPV E6/E7 messenger RNA expression profile shows a better correlation with the severity of the cervical lesions. Hypermethylation of cellular genes, repressing their transcription, especially the E-cadherin expression, prevent HPV-infected cells to be cleared by the immune cells, allowing a persisting infection and the progression to high-grade lesions and cervical cancer. Intracellular noncoding microRNA reduce genes expression by bounding to messenger RNA. Alterations of miRNA levels, triggered by E6/E7 oncogenes, could contribute to cancer development.

**Keywords:** HPV, biomarker, cervical cancer screening

## Imagistic correlations between ultrasound and MRI examination of the fetus with congenital diaphragmatic hernia

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**Introduction.** We wanted to find correlations between the ultrasound examination of pregnancies with diaphragmatic hernia and the MRI examination that followed in these cases. Fetal MRI is used to confirm, complete and make the differential diagnosis in difficult cases. In some cases, it can also bring forth new information regarding the prognosis. **Materials and method.** This was a retrospective study of six pregnancies that were recommended to a third-degree maternity from multiple diagnosis centers. The ultrasounds and MRI examinations were performed in specialized fetal medicine study centers. The information obtained about the progression of pulmonary hypoplasia helped decide the prognosis and treatment of these cases. **Results.** The diagnosis was made in the second trimester in four cases and in the third trimester in the other two cases. We described the herniated organs, the dimensions of

the hernia, and the remaining lung capacity, so that we could correctly evaluate the prognosis. We also used the lung-to-head ratio (LHR) to try to determine better the degree of lung hypoplasia. **Conclusions.** Considering diaphragmatic hernia as a solitary malformation, the localization (on the left side, right side, or bilateral) corresponds with the international statistics. High-quality ultrasound followed by an MRI examination helped correctly appreciate the prognostic, treatment possibilities and the total affected lung volume. With the expansion of highly specialized fetal medicine study centers, there will be an increase in the diagnosis capacity. The MRI follow-up will increase the certainty of the diagnosis and improve the overall quality of the medical care.

**Keywords:** fetal diaphragmatic hernia, fetal abnormalities, prenatal diagnosis, ultrasound examination, fetal MRI

## Therapeutic approach to managing menopause

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Most women who transition menopause experience a wide range of bothersome symptoms and many require immediate treatment to maintain a good quality of life. But the kind of treatment that best suits each one of them and the decision to use hormone therapy (HT) need to balance the benefits against the potential risks. Despite the controversy and given the persistent confusion about HT, either estrogen alone or estrogen combined with progestin is the most effective treatment for menopausal symptoms. The most prevalent symptoms of menopause are vasomotor symptoms, such as hot flashes and night sweats, as well as genitourinary dysfunction with vaginal or vulvar dryness, discharge, vaginal atrophy and dyspareunia. Also, not to be ignored, low self-esteem, depression and anxiety are major signs of an impaired life quality and are likely to be improved by HT. Short-term estrogen

therapy no more than five years and the lowest effective dose are considered for moderate to severe menopausal symptoms. Some women may need long-term therapy for severe, persistent symptoms to whom alternatives such as selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, GABA-ergics or  $\alpha_2$  adrenergic receptor agonists may be more suitable. HT should not be prescribed without a clear indication; the efficacy and dosage should be assessed annually. Risks and benefits differ for women transitioning menopause than for older women far from last menstrual period. The mode of delivery should be tailored to each woman's risk profile and personal preference. Menopausal HT should be part of a healthy lifestyle, including physical exercise, diet, smoking and alcohol cessation.

**Keywords:** menopause, hormone therapy, vasomotor symptoms, estrogen, lifestyle, risks, benefits



## Impact of COVID-19 on pregnancy services

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Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a rapidly evolving pandemic. Roughly two-thirds of pregnant women with COVID-19 have no symptoms at all, and most pregnant women who do have symptoms have only a mild cold or flu-like symptoms. Pregnant women are more susceptible to viral infections due to immune and anatomic factors. The main challenge will be maintaining the provision of emergency and obstetric care, while preserving the already scarce

resources. Maternity services must face extreme challenges during the pandemic. In addition to caring for the pregnancy outcome, the obstetricians deal with various challenges, especially regarding monitoring pregnancies in a context with difficult access to healthcare services. Two complicated cases will be presented, one due to the lack of investigations of the fetus, and the second one due to poor investigations of the pregnant woman.

**Keywords:** pandemic, COVID-19, health services, pregnancy outcome

## News on HPV infection of uterine cervix

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High-risk HPV strains infection is the cause of cervical cancer. Screening based on cytology dropped the incidence and mortality by 80% in the countries where it was implemented as a national health policy. In the last years, it has been clearly revealed that the sensitivity of the screening cytology is diminishing after menopause. Many studies revealed that HPV primary screening is a more accurate way to detect women with a high risk of developing precursor lesions and, later, cervical cancer. Not all the high-risk HPV strains have the same risk to induce precancerous lesions. There is a risk stratification of high-risk HPV. The highest risk is related to 16, 18,

31, 33 and 45 strains. There is a need to make a triage for HPV high-risk strains. A newer method of triage for HPV primary screening is the dual stain cytology. This technique is based on the simultaneously search of p16 and Ki-67 expression as an indicator of dysplastic cervical cells. This triage technique will be associated with fewer colposcopies, a better detection of CIN3+, fewer biopsies and with a better reassurance for women tested negative. Romania needs a national cervical cancer screening program and this should be based on HPV primary screening.

**Keywords:** HPV, cervical cancer, cytology, screening

## Treatment and prophylaxis with tranexamic acid in obstetric hemorrhage

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Obstetric hemorrhage represents the most common cause of maternal mortality and morbidity. The incidence of post-partum hemorrhage is 6-10%, being responsible for approximately 100,000 maternal deaths per year. The average interval from onset of bleeding to death is 2 to 4 hours. A Cochrane review revealed that tranexamic acid reduces blood transfusion in patients undergoing emergency non-obstetrical procedures; its half-life is about 2 hours. Tranexamic acid is a lysine analogue which inhibits the binding of plasmin and plasminogen to fibrin, acting like an antifibrinolytic. Antifibrinolytic agents have been extensively studied

and are recommended in multiple medical fields, especially in traumatology and cardiovascular surgery. Due to the status of hypercoagulability described in pregnancy and in postpartum period, the reluctance to use tranexamic acid has prompted numerous clinical trials that have demonstrated its efficiency in the obstetric field. The World Health Organization has updated the recommendations of tranexamic acid due to its efficiency, showed by numerous studies, both in the prophylaxis and treatment of postpartum hemorrhage.

**Keywords:** postpartum hemorrhage, tranexamic acid, antifibrinolytic agents

## New approaches to predicting and diagnosing preeclampsia – Congo red dot test paper

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Preeclampsia is a pathology of pregnancy characterized by the appearance of hypertension and de novo proteinuria, currently burdened by a high mortality, affecting, on average, 2.5-7% of single pregnancies and 7-21% of general pregnancies. With an incompletely known pathophysiological substrate, the diagnosis of preeclampsia is currently based on traditional clinical markers, unfortunately uncertain and non-specific. Hoping to develop an affordable and simple procedure for diagnosing preeclampsia, Buhimski et

al. started with the idea of using the Congo red to highlight structurally modified proteins in the urine of women with preeclampsia. This feature of staining has an important potential for diagnosis and prognosis, because it can build up the presence in the urine of altered proteins before the onset of the clinical manifestations, also correlating with the severity of the disease.

**Keywords:** Congo red, preeclampsia, congophilia, misfolded proteins

## Acute respiratory distress syndrome (ARDS) in pregnancy caused by SARS-CoV-2

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**Introduction.** Since December 2019, SARS-CoV-2 has spread worldwide and became pandemic, with a huge impact on medical and social life everywhere. The information about its effects during pregnancy are still limited. The purpose of our study was to reveal the main characteristics of acute respiratory distress syndrome (ARDS) in pregnancy caused by SARS-CoV-2 infection.

**Methodology.** We reviewed the main medical databases, such as PubMed, MEDLINE and Web of Science, searching publications about SARS-CoV-2 in pregnancy, and we focused on reports about the respiratory symptoms, such as ARDS. **Results.** Our research revealed 1621 articles about SARS-CoV-2 infection and pregnancy. The studies are focused on clinical characteristics, biologic maternal changes and fetal outcome. Where the universal testing was available, asymptomatic infection occurred in 43.5-92% of pregnant women. In

the majority of studies, the severe and critical COVID-19 illness rates were similar to those of the nonpregnant population. There are few data based only on ARDS caused by SARS-CoV-2 in pregnancy. But the reported cases were in the second or third trimester of pregnancy and the respiratory symptoms resolved in a median of 24 days. It was proved that obesity and COVID-19 may increase the risk for induced preterm birth to improve the maternal pulmonary status in late pregnancy. These findings characterize pregnant patients as a higher-risk group, mainly those with chronic comorbidities. **Conclusions.** Acute respiratory distress syndrome cause by SARS-CoV-2 infection in pregnancy is a severe condition, with both maternal and fetal consequences, especially in patients with comorbidities.

**Keywords:** ARDS, SARS-CoV-2, pregnancy, preterm birth

## COVID-19 vaccination in pregnancy and breastfeed period – pro and con arguments

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**Introduction.** In less than a year after the identification of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19), vaccines are beginning to be distributed worldwide. Six leading vaccines are available at the moment. **Methodology.** We searched the medical databases, such as PubMed, MEDLINE and Web of Science, searching for publications about COVID-19 vaccines in pregnancy and the current recommendations. **Results.** Our research revealed 54 publications about COVID-19 vaccines in pregnancy. Due to the exclusion of pregnant women from the initial phase 3 clinical trials of COVID-19 vaccines, limited data are available about the safety during pregnancy. International and national maternal-fetal organizations and obstetricians' societies have analyzed the recent data. The information included results from animal studies and inadvertently

exposed pregnancies during vaccine clinical trials. The results show that pregnant women may be taken in consideration for COVID-19 vaccination. The obstetrician remains the key consultant who must expose the potential risks to pregnancy of vaccine reactivity, evidence for the safety of other vaccines during pregnancy, the timing of vaccination during pregnancy, the risk of COVID-19 complications due to pregnancy and the pregnant woman's underlying conditions, and the risk of exposure to severe acute respiratory syndrome caused by SARS-CoV-2, along with the potential for risk mitigation. **Conclusions.** National obstetrician societies have issued supportive guidance of offering COVID-19 vaccine to pregnant women. As additional information becomes available, it will be critical for obstetricians to keep up to date with this information.

**Keywords:** SARS-CoV-2, pregnancy, vaccine

## Timing neuroprotection in perimenopause

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Endocrine and neural senescence overlap, by intertwined complex feedback loops. The variable levels of estradiol, progesterone (P4), DHEA-S and neurotransmitters – GABA, serotonin, dopamine and glutamate – are dependent on sex steroids, that make the women's brain to suffer from menarche to menopause. Perimenopause to menopause transition (MT) is a critical period, a neurological transition state, offering a window of opportunity to delay brain aging/neurodegenerative diseases onset, such as Alzheimer's disease (AD). Hot flushes, sleep disorders and depression are alarm signs of missing estrogens, a "master regulator" of brain's glucose metabolism (transport, aerobic glycolysis, insulin resistance, mitochondrial function to generate ATP), from multiple cognition areas. The longer duration of estrogens deprivation jeopardizes neurons' structure and functions, and indirectly brain synapses, favorizing brain bioenergetic crisis, with aggregation and deposition of amyloid, hippocampal and prefrontal cortex volume loss during perimenopause to MT, accentuated when having a history of obstetrical major

syndromes. Depression associated with verbal and working memory, learning and cognition disorders are present from the earlier ages in case of oophorectomy/premature menopause. Aβ oligomers plus fibrils accumulation, as well as metabolic and inflammatory changes of dementia have onset in the early years of menopause, this being the moment to start hormone therapy (HT) for neuroprotection, demonstrated by animal models, observational/RTC studies. Estradiol protects neurons from excitotoxic damage and increases neuronal survival, compared to tamoxifen and anastrozole. Progesterone, allopregnanolone – P4 5α-reduced metabolite, stimulate neurological and functional recovery, different from progestogens. Androgens exhibit neuroprotection in motoneurons, supporting cell survival, axonal regeneration and dendritic maintenance. One must individualize HT to the woman's characteristics, because estrogens, progestogens and androgens are not all the same.

**Keywords:** perimenopause, critical window of opportunity, neuroageing, neuroprotection, sex steroids

## Caesarean section surgery in the 21<sup>st</sup> century

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Caesarean section is the most common surgery performed in the world. In the last decades, Romania has reported an increasing trend in caesarean sections. The number of caesarean sections in Romania is among the highest in the EU; an increasing trend of 32.1% was reported between 2009 and 2017. Although the World Health Organization does not recommend any longer an ideal rate for caesarean sections, the pragmatismal range of 10-15% at the population level is used for monitoring, aiming to ensure maternal and perinatal health benefits and reduce potential harms. Since the first instructions on how to perform the caesarean technique in 1480, a radical improvement of surgical technique, but also in enhanced recovery was done. The technique was simplified in order to reduce the intraoperative blood loss and the operating time. The occurrence of the iatrogenic "scar pregnancy" and "adherent morbidly placenta" as a major complication at high risk of maternal mortality

and morbidity made us reflect on the most appropriate surgical technique in order to avoid major complications. Also, the primacy of obstetric indications and the easy choice of caesarean section for childbirth method made us want to perform a fast operation, with a favorable evolution. The objectives of this presentation are: 1) pre-operative and postoperative recommended management of the patient; 2) to discuss different surgical techniques regarding skin incision and closure, uterine incisions, closure versus non-closure of the peritoneum; 3) to analyze the techniques of fetal extractions, including difficult fetal extractions. In conclusion, the caesarean section technique may use surgical technical aspects supported by medical evidence in order to decrease the short- and long-term maternal and fetal morbidity and mortality.

**Keywords:** surgery, caesarean section, uterine incision, fetal extraction

## Update regarding breast cancer screening

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Breast cancer is the most common type of cancer occurring in women and the second most common cancer overall. The breast cancer incidence forecast by 2025 reveals a trend of continuous growth of new breast cancer cases, which requires an increased attention to the early detection of this disease through screening that would lead to a reduction in costs and mortality. Because the chances of cure depend very much on the time/period of diagnosis, most European countries have adopted effective breast cancer screening programs. Introducing mammography as a screening method has led to a reduction of mortality in breast cancer with 30%. Traducere în Engleză. Digital mammography with tomosynthesis (3D mammography) represents the cutting-edge technology in the detection of breast lesions and, at this time, it is the most modern technique of screening and diagnosis of breast cancer in early stages. Classical mammography

represents an exposure on a simple radiological film, while digital mammography is done on digital, electronic media, and some of the advantages are represented by an increased sensitivity, lower radiation dose and higher resolution. It's not always possible to distinguish between a benign and a malignant tumor and it's not possible to specify the nature of an image, thus being absolutely necessary to complete the exam with a mammary ultrasound or a magnetic resonance imaging scan in order to establish the diagnosis. The widespread use of mammographic screening, with huge benefits all over the world, depends on the technique, the films and the quality of the equipment. Despite its limitations, mammography remains a vital tool in breast cancer screening, being able to recognize incipient changes with high sensitivity in postmenopausal women.

**Keywords:** breast cancer, screening, mammography

## The road to ovarian cancer screening

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In the last years, one of the main medical objectives of gynecology was successfully identifying early-stage ovarian cancer. Because of its low sensitivity, CA125, traditionally the main ovarian cancer biomarker, cannot be used in early-stage screening. Nowadays, there is a constant search to identify new biomarkers that could be used individually or mixed together to create a screening test for incipient ovarian cancer. A series of reports

suggest that Pap test fluid can be used to track specific ovarian cancer biomarkers. Although a large number of proteins or protein fragments have been identified as potential ovarian cancer biomarkers, no agreement has been reached yet to introduce a new universal screening test.

**Keywords:** ovarian cancer, screening, biomarker, CA125, smear test

## Detailed genetic testing in fetuses with structural anomalies

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**Introduction.** Whenever a structural fetal anomaly is detected and there is an indication for genetic testing, conventional methods, including rapid tests (QF PCR), cytogenetic karyotype and molecular karyotype (CGH), are able to detect an underlying genetic problem in around 40% of cases. **Aim.** Our purpose is to investigate whether newer genetic tests are more efficient in detecting a genetic cause for specific fetal malformations. **Materials and method.** We searched the literature for publications regarding the use of next-generation sequencing (NGS) tests in postnatal and antenatal cases with developmental problems. **Results.** The largest registry including children with developmental disorders and their families is based in UK (DDD – Deciphering Developmental Disorders) and publishes regular reports on the efficiency of WES (whole exome sequencing) testing, which reaches 40% in cases where conventional

techniques failed to find a diagnosis. Similar testing in an antenatal setting showed poorer results, with an average of 12.5% diagnosis rate. **Discussion.** The much lower than expected results rate in antenatal setting may be explained by a different patient selection. One of the most common features that prompt for genetic testing postnatally is delayed neurological development. This feature is not available for antenatal detection. The main criterion for patient selection antenatally is represented by a structural malformation or growth restriction. **Conclusions.** There is a place to investigate whether mild fetal anomalies, such as borderline ventriculomegaly or isolated agenesis of corpus calosum, may carry the potential of a later neurodevelopmental disorder and be associated with a targeted genetic anomaly.

**Keywords:** structural fetal anomaly, WES, antenatal genetic testing

## Umbilical cord blood gas analysis – a valuable marker of perinatal hypoxia-ischemia

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**Introduction.** Blood gas analysis (BGA) of samples taken from the umbilical cord after expulsion represents an immediate evaluation method of fetoplacental circulation evaluation and hypoxic-ischemic risk assessment. **Materials and method.** Based on the most recent bibliographic references, this study reflects the experience of certain medical teams that bring evidence and reason to support this investigation and, as a consequence, have imposed its use in a systematic manner. The technique of venous and arterial blood umbilical cord sampling immediately after birth is described. **Results and discussion.** Initially, the normal values of the BGA parameters in a healthy newborn are presented. Further on, the pathological changes of these samples suggest the following: the blood taken from

the umbilical arteries reflects the newborn's condition and the one taken from the umbilical vein reflects the placental status. The arterial and venous base deficit can detect the severity of the metabolic or mixed acidosis. Compared to other fetal and neonatal monitoring methods, the present one is accessible, noninvasive, cheap, but also safe. **Conclusions.** This study aims to present arguments and indisputable evidence which recommend this exploration as a suitable method in the current clinical practice, as a means of newborn monitoring immediately after expulsion. The results of this analysis can be subsequently used to prove the quality of perinatal management and/or as documents in case of malpractice litigations.

**Keywords:** blood gas analysis, perinatal management

## Immaturity of the digestive system of the premature baby – clinical and nutritional implications. Clinical case

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In the process of caring for the premature baby, we try to emphasize all the necessary acquisitions in the last trimester of pregnancy or earlier. The existence of an "opportunistic consumer" *in utero* does not always help him in the early postnatal adaptation. The development of the gastrointestinal system in the premature newborn in the last trimester is important both regarding the accumulation of necessary nutrients and the normal neurological growth and development. This system is an in and out "harbor" for general growth. An optimal parenteral nutrition influences on short term the somatic growth, the efficient tissue development and the normal

bone density, but also prevents the occurrence of major complications, such as ulcero-necrotic enterocolitis. Food intolerance and ulcero-necrotic enterocolitis have their origin in the disturbance of normal anatomical and physiological development in the premature newborn. Thus, we bring to your attention the case of a premature newborn of 31 weeks who presented from the third day of life hematochezia and abdominal distension. In this case, clinical and paraclinical evaluations in series were the secret of the favorable evolution.

**Keywords:** digestive system of the newborn, preterm nutrition

## Fetal and neonatal alloimmune thrombocytopenia: early antenatal diagnosis leading to successful management after birth in the second pregnancy – case report

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Fetal and neonatal alloimmune thrombocytopenia is one of the main causes of severe thrombocytopenia present at birth. It is characterized by fetomaternal alloimmunization against fetal antigens inherited from the father. It has an estimated incidence of 1 case/2500 births and the main goal is to prevent the occurrence of severe complications, such as intracra-

nial hemorrhage, neurodevelopmental impairment and death. This case report demonstrates the importance of antenatal diagnosis for the prevention and proper management of the fetus and newborn in the second pregnancy.

**Keywords:** neonatal thrombocytopenia, fetomaternal alloimmunization, intracranial hemorrhage

## Congenital hepatic vascular malformations: diagnostic and therapeutic aspects

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Congenital vascular anomalies of the liver are abnormal vascular connections appeared between the 4<sup>th</sup> and 10<sup>th</sup> weeks of gestation. These are driving the blood through arteriovenous communications between portal vein, hepatic artery and hepatic vein, this way by-passing the hepatic capillary circulation. There are described portal systemic venous shunts, arteriovenous and arterioportal, which are usually interesting only one hepatic lobe. The incidence is difficult to evaluate, sometimes these remaining underdiagnosed. The clinical presentation could be as heart failure and hydrops fetalis, portal hypertension, liver failure, microangiopathic hemolytic anemia, thrombocytopenia and consumption coagulopathy (Kasabach-Merri-

sequence). There are forms which associate persistent pulmonary hypertension. Some forms associate metabolic disorders, such as transitory galactosemia, hyperammonemia, and transitory neonatal cholestasis. Ultrasound evaluation shows dilated vessels, tangle of tortuous vessels localized at the level of a single lobe and arterialization of hepatic venous circulation. The diagnosis requires a multidisciplinary team: neonatologist, radiologist, surgeon. In this paper, we are presenting the clinical, diagnostic and therapeutic aspects of some cases of arteriovenous malformations born in our service over a period of three years.

**Keywords:** vascular malformations, arteriovenous shunts, liver failure

## Neonatal hypoxic-ischemic encephalopathy – specific lesions in the premature newborn

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**Introduction.** Increasing the incidence of prematurity and the recovery of the premature newborn at a smaller gestational age have led to an increase in neurological disorders caused by hypoxic-ischemic injuries, grafted on the immature or extremely immature brain. Progressive hypoxemia associated with hypercapnia and metabolic acidosis cause multiple multiorgan lesions, with early neurological manifestations: convulsions, apnea, hypotonia, coma. **Objective.** An analysis of major neuropathological factors and clinical-evolutionary consequences, imagistically documented, in lesions specific to prematurity caused by neonatal asphyxia. **Materials and method.** Documented analysis of neuropathological patterns of neonatal hypoxic-ischemic encephalopathy. In the premature newborn, predominate periventricular leukomalacia and the marbled status of the basal ganglia and the thalamus. **Results.** Because 80-90% of periventricular leukomalacia cases occur in the premature newborn, a direct correlation was established

between the high frequency of the disease, the degrees of cerebral immaturity, and the history of hypoxia or perinatal asphyxia. In the newborn resulting from laborious births, obstetric traumas and severe neonatal cardiorespiratory pathology, the incidence is higher. Changes in cerebral circulation, cerebral velocity, the systemic hypotension, and the coagulation disorders cause in the first stage a coagulation necrosis of the white periventricular substance located at the external angle of the lateral ventricles, in the area of intersection of the terminal branches of the middle cerebral artery with choroidal arteries. Depending on the dimension and the evolution of the lesion, the clinical signs will occur, as well as the complications. **Conclusions.** Extreme prematurity associated with hypoxemia and metabolic acidosis are risk factors for hypoxic-ischemic encephalopathy, respectively specific lesion periventricular leukomalacia.

**Keywords:** periventricular leukomalacia, premature newborn

## Difficulties in the nutritional recovery of the newborn with digestive tract malformation

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**Introduction.** Congenital anomalies of the digestive tract occur during the embryonic development. The cause of these malformations is still unknown, although some experts believe that there may be a genetic link.

**Objectives.** The evaluation of postoperative nutritional recovery compared to healthy newborns. **Materials and method.** A retrospective study was performed, for a period of 12 months (1.01.2020-31.12.2020), in which there were introduced all the newborns with gastrointestinal malformation operated and hospitalized in the Neonatology-Premature Department of the "Louis Țurcanu" Emergency Clinical Hospital for Children, Timișoara. The following parameters were analyzed: admission weight and discharge weight, duration of the hospitalization, postoperative diagnosis, and the moment of starting enteral feeding. **Results.** Out of a total of 20 confirmed cases, those located in the small intestine were 8 (40%), one case being associated with jejunal-jejunal fistula, and 7 congenital malformations of the esophagus, of which three were associated with esophageal fistula.

There were two cases of malformations of the upper digestive tract (10%), and three newborns (15%) presented malformations of the large intestine. The rate of nutritional recovery was slow, 35% had malabsorption syndrome, 15% required replacement of the gastrostomy, and 10% of cases required surgery reinterventions. Enteral feeding started differently, depending on the type of malformation, and was performed from the second day to the 10<sup>th</sup> postoperative day. All newborns received additional hydroelectrolytic rebalancing infusions. With the daily increase in the amount of milk, the need for infusions decreased. **Discussion and conclusions.** Early enteral feeding can increase survival, accelerate the recovery of gastrointestinal function and improve nutritional status in the newborn. The management of a fetus with a gastrointestinal malformation should include a qualified staff to administer the diet, nutritional recovery being much slower and the complications being more frequent.

**Keywords:** digestive tract malformation, enteral feeding, nutritional recovery

## Autoimmune disorders in pregnancy and their impact on the neonate

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Autoimmune disorders are a group of chronic diseases with multifactorial determinants, some having genetic predisposition, while others may occur sporadically. During pregnancy, there are various physiological changes (increased basal metabolic rate, weight gain, hormonal changes) that can be a trigger for the development of an autoimmune disease. This pathology has been linked to obstetric complications, such as pregnancy loss or preterm delivery. Autoimmune diseases

prevalence is around 7-9% of the world population, with an incidence two times higher among women. In 2020, in our department, their prevalence was around 2%. The authors propose a review of the most common autoimmune diseases encountered in pregnancy, with the presentation of two particular cases which required intervention.

**Keywords:** autoimmune diseases, pregnancy pathology, neonatal immune pathology



## Cerebral fetal destructive process – case presentation

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Among cerebral anomalies in neonate, the early detected cystic lesions are a consequence of destructive processes that may occur any time in gestation, particularly in the third trimester, and most of these are the consequence of vascular accidents, hemorrhage or occlusion. The etiology is unknown, with a variety of obstetric complications, such as placental insufficiency, coagulation disorders, drug consumption and transplacental infections. Prenatal stroke is considered the most important determinant of cystic destruction of the cortex. This type of lesions may have severe consequences, but they sometimes may escape the early detection, in the absence of neurological anomalies. We present a case of a term baby with IUGR, 2050 g, born from an uninvestigated pregnancy at 38 weeks, from a normal pregnancy, according to the mother (she is a smoker, denying any toxic or drug abuse), extracted by

caesarean section, due to mother's preeclampsia, with entangled cord, Apgar scores 6/8. The baby required resuscitation at birth, but other than that, there were no other interventions. The clinical examination at birth showed no other anomalies, except for microcephalia (PC – 29 cm <p5). The clinical course was normal, except for the prominency of cranial sutures. The ultrasound examination showed multiple cystic destructions in the frontoparietal area. The case raised problems of differential diagnosis regarding the origin of the brain injury. The aforementioned lesions do not correspond to any arterial territory, nor to the typical venous stroke. The MRI aspect would rather be characteristic to periventricular leukomalacia, in the context of perinatal parenchymatous injuries in a hypoxic environment.

**Keywords:** cerebral cystic destructions, IUGR, microcephaly

## Newborn with hemolytic disease – hereditary etiology and case presentation

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The diagnosis of hereditary spherocytosis in a newborn infant was given at birth, in context of a positive family history. The signs and symptoms are highly variable. The disorder may escape the clinical recognition or in other cases anemia and hyperbilirubinemia could be severe and require intensive phototherapy and sometimes early erythrocyte transfusions. V.A. was born at 38 weeks, from a normal pregnancy, weighing 3000 grams, with Apgar scores 9/10, and she appeared healthy, with no dysmorphism features. In the first 12 hours, she was noted to be jaundiced and phototherapy was recommended. Both mother and baby were B III (+) and the direct antiglobulin test was negative. In the context of a family with positive anamnesis, congenital spherocytosis was suspected. Baby's blood tests showed hyperbilirubinemia, elevated

MCHC, normal MCV and anisocytosis, spherocytes and reticulocytosis on the peripheral blood smear. During hospitalization, she required prolonged phototherapy, administration of albumin, and when anemia appeared, she was transfused. During the next several months, RBC transfusions were administrated every 2-3 weeks. **Discussion.** When evaluating a neonate with Coombs – negative, hemolytic jaundice, with a positive family history of spherocytosis, the presence of spherocytes on blood film and high MCHC suggested the diagnosis of hereditary disease. Children diagnosed early in life usually prove a severe form of hemolytic spherocytosis that results from such an early presentation.

**Keywords:** hereditary spherocytosis, severe jaundice and anemia

## Controlled hypothermia – the main neuroprotective strategy in newborns with moderate or severe perinatal hypoxia

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Perinatal hypoxia is a condition characterized by decreased oxygenation of tissue and organs, resulting from a hypoxic or ischemic event happening peripartum or intrapartum. Neonatal encephalopathy is the main manifestation of perinatal hypoxia and is manifested by neurological dysfunction in the first days of life of the late preterm or full-term newborn. The high incidence rate of encephalopathy (3/1000 live term births) that associates high mortality (15-20%) and morbidity rates (permanent neurologic deficits – 25%) has led to the development of new and efficient management strategies regarding perinatal hypoxia. Controlled neonatal hypothermia is currently the main management strategy for moderate-severe perinatal

hypoxia, proving to have a neuroprotective role and minimizing brain damage, if initiated in the first six hours of life. Significant progress has been made in identifying predisposing factors and in the early detection of perinatal hypoxia. A thorough analysis of the risk factors for the development of hypoxic-ischemic encephalopathy can signal the pathology and improve the survival rates of the newborn through the early initiation of treatment. The focus of this presentation is controlled hypothermia as a neuroprotective measure in the therapeutic management of moderate or severe perinatal hypoxia.

**Keywords:** perinatal hypoxia, hypoxic-ischemic encephalopathy, controlled therapeutic hypothermia

## Neonatal meningitis with *Candida albicans* in a premature baby

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Fungal infections among neonates are relatively rare and they are usually located at the cutaneomucosal site. In the neonatal intensive care units (NICU), *Candida* species are important pathogens, especially in very low birth weight (VLBW) infants, where they represent the cause for 1.4% of early onset sepsis and 2.6% up to 16.7% in VLBW and 20% in extremely low birth weight (ELBW) babies with late onset sepsis. Invasive candidemia can result from the infant's endogenous flora or from nosocomial transmission and can disseminate in different organs (kidney, heart, eye, central nervous system). The clinical picture consists in signs and symptoms similar to those of bacterial sepsis, but with a higher mortality (up to 24% of the cases). We present a case of a very-low-birth-weight (VLBW) premature baby with respiratory distress and infectious risk associated to pregnancy who was admitted in the neonatal intensive care unit for respiratory support and intravenous antibiotic therapy and, despite the prophylactic administration of fluconazole, at 7 days of

life he was diagnosed with sepsis with *Candida albicans*. The cranial US showed multiple diffuse hyperechoic lesions associated with neurological alterations. Cerebrospinal fluid cultures were negative, but the clinical and imaging signs supported the diagnosis of fungal meningitis, and the baby was switched on treatment with caspofungin. The clinical course of the disease was slowly favorable, with the disappearance of the cerebral lesions. The baby was discharged at 2 months of age, in good condition and without short-term disabilities. **Conclusions.** Premature birth and long-term, broad spectrum antibiotic therapy along with central catheterization are factors that increase the risk for systemic fungal infections, despite prophylaxis. Cerebral secondary determinations usually predict a poor prognosis, but with the correct treatment (sensitivity, doses and duration), the outcome can be favorable, with *restitutio ad integrum*, without disabilities.

**Keywords:** neonatal meningitis, fungal infections in neonate, *Candida albicans* meningitis

## Alternative strategies in the treatment of neonatal sepsis

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Neonatal sepsis is a severe condition, frequently diagnosed in the neonatal intensive care units (NICU). Late-onset sepsis is usually nosocomial, with multiresistant germs, or sometimes remains a clinical diagnosis, with negative bacteriologic tests. In these cases, the therapeutic strategies depend on local flora sensitivity and the physician's experience. A different approach could be the continuous administration of antibiotics versus classic intermittent posology, as it may present several advantages and less toxicity. We realized a review of literature and among several recent articles, regarding the optimum way of prescribing antibiotics, considering their pharmacokinetic properties. There is a group of antibiotics – beta-lactams, carbapenems, vancomycin, linezolid, cephalosporins (called time-dependent) – which are efficient as long as their plasmatic concentration remains above the minimum inhibitory concentration (MIC) for microorganisms, while other groups (aminoglycosides, fluoroquinolones) are dose-dependent – their efficacy is related to the ratio between their peak concentration and

MIC. These properties reflect in the fact that, for the first group, one should prolong the time of administration in order to increase their killing activity, while for the second group, increasing the dose may help improving their efficiency. For the time-dependent antibiotics, the continuous infusion instead of intermittent administration was proven to be superior in terms of clinical response. This strategy may represent, therefore, an alternative for the management of severe cases of sepsis which do not respond to the classical approach. **Conclusions.** The consequences of late-onset sepsis can be devastating, with life-threatening complications and, therefore, the interventions should be prompt and aggressive, especially for very immature and immunocompromised babies and for critical patients with central lines that cannot be removed. The continuous infusion of antibiotics may be advantageous, with better efficiency and fewer side effects.

**Keywords:** continuous antibiotic infusion, time-dependent antibiotics, concentration-dependent antibiotics

## Respiratory distress syndrome (RDS) and cytomegalovirus (CMV) pneumonia in an ELBW premature baby

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Cytomegalovirus (CMV) infections in neonates can be transmitted transplacentally (congenital infection), perinatally (genital secretions) or postnatally (mother's milk, transfusions). Almost 10% of the patients are symptomatic, the risk being higher with lower gestational age. Depending on the type of the infection, the clinical picture can vary, from a multisystemic disease to isolated specific signs or late neurosensory sequelae. Milder or incomplete clinical presentations and associated pathology can raise problems of differential diagnosis and management. We present a case of extremely-low-birth-weight (ELBW) premature male baby, at 29 weeks of gestation, weighing 650 g, with intrauterine growth restriction (IUGR) and prenatal diagnosed chromosomal anomaly, who developed respiratory distress syndrome (RDS) and recurrent isolated thrombocytopenia, being admitted in the neonatal intensive care unit and treated with surfactant, mechanical ventilation, antibiotics, supportive therapy, with an unfavorable course of his condition, requiring long-

term respiratory support and hospitalization. The clinical picture was dominated by the respiratory signs and symptoms, with no significant jaundice, hepatosplenomegaly or hemorrhagic events. The serologic testing for TORCH syndrome in pregnancy was not performed, but the baby's results revealed positive IgM anti-CMV and active viral replication. Although the treatment with ganciclovir was considered, at 36 weeks postconception, the clinical and radiographic signs supported the diagnosis of chronic lung disease, which despite the different therapeutic strategies was complicated with pulmonary hypertension, cor pulmonale, and the baby died at 4 months of age. **Conclusions.** The association of a congenital chronic infection with prematurity is an aggravating factor for developing chronic lung disease. The screening in pregnancy for the CMV infection is extremely useful for a prompt diagnosis and for an appropriate management.

**Keywords:** CMV pneumonia, congenital CMV infection, TORCH syndrome

## Thrombocytopenia assesment in the neonate

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**Objective.** To review the main types of diseases causing thrombocytopenia and to discuss the best methods for selecting the candidates for the transfusion of thrombocytes. **Methodology.** The definition of thrombocytopenia in the neonate uses the same criterion as for the adult, that is a number of platelets less than  $150 \times 10^3 / \text{mm}^3$ , a level that corresponds with the 5<sup>th</sup> percentile for the adult population. In the neonate, the 5<sup>th</sup> percentile for this parameter has lower values (around  $120 \times 10^3 / \text{mm}^3$  in term neonates and about  $100 \times 10^3 / \text{mm}^3$  in pre-term neonates born before 32 gestational weeks). Thus, a larger proportion of the neonatal population will be diagnosed with thrombocytopenia, although the neonatal platelets seem to provide normal function even with

lower numbers. The platelet transfusion is administered in neonates with moderate or severe thrombocytopenia, taking into consideration various clinical situations in order to choose the threshold for transfusion, but the threshold is nevertheless higher than in children and adults. Moreover, the transfusion itself is not without risks, and the decision to administer it should be very well documented. **Conclusions.** New laboratory tests, such as platelet function analyzer and immature platelet fraction, can help in the future for both selecting the patients with enough platelets activity and to set new lower thresholds for those transfused.

**Keywords:** thrombocytopenia, neonate, platelet transfusion, immature platelet fraction

## Noninvasive versus invasive respiratory support in respiratory distress with surfactant deficiency

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**Introduction.** Prematurity is a major public health problem. Despite improvements in pregnancy monitoring techniques, diagnosis and prenatal treatment, prematurity is an important cause of neonatal morbidity. **Aim.** The evaluation of respiratory support in the first three days of life in neonates with prematurity of less than 32 weeks. **Materials and method.** This paper is a descriptive study on the variability of respiratory support during the first three days of life in premature newborns hospitalized in the intensive care unit of the Neonatology Department of the County Emergency Clinical Hospital of Cluj-Napoca, between November 2009 and July 2020. **Results.** The study group had an average weight of  $993.12 \pm 110$  g and 27.782.3 weeks of gestational age. 66% of newborns were less than 1000 grams at birth. 76.8% had pregnancy pathology, the most common being maternal infection. 72% of cases received a complete treatment with dexamethasone. The first dose of surfactant

was given to 15 newborns. On the first day of life, nCPAP was applied in 13 cases in the same way as SIMV support. The evolution was towards the decrease of the support on the second day and on the third day of life. On the nIPPV support, the utilization rate gradually increased from day 1 to day 3. On day 1, SIMV predominated at gestational ages of 24-27 weeks, and at 28-33 weeks the nCPAP support predominated. For the second day, in the group of 24-27 weeks, SIMV type support predominated, but almost noninvasive nIPPV support was provided. On the third day of life, in the 24-27 weeks group, nIPPV type support predominated and in the 28-33 weeks group, nCPAP and oxygen predominated. **Conclusions.** Extreme prematurity requires invasive respiratory support on the first day of life. In the next two days, the need for non-invasive support predominates.

**Keywords:** respiratory support, prematurity, surfactant

## Neurological complications in preterm infants

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**Introduction.** More than 1 in 10 infants are born preterm every year. Preterms are the infants born before 37 weeks of gestation and weighing less than 2500 g at birth. Some of them face important and long-lasting neurodevelopment problems. **Objective.** The objective of this study was to calculate the incidence of prematurity over the years 2016-2017 and the incidence of neurological complications in premature neonates in this group. **Materials and method.** For the elaboration of this paper, a retrospective cohort type observational study was carried out on a two-year period, 2016-2017, at the Bega Neonatology Department of the "Pius Brinzeu" County Emergency Clinical Hospital in Timișoara. The criteria were represented by preterms with HIE and/or intraventricular haemorrhage. **Results and discussion.** A total of 183 of the 904 premature infants devel-

oped neurological complications. These complications occurred most frequently at the gestational age of 30-32 weeks, and the lowest percentage for gestational age was between 24 and 26 weeks. Regarding neurological complications, the most frequent ones were hypoxic-ischemic encephalopathy and intraventricular haemorrhage (IVH). Regarding IVH, most of the cases developed a grade II, followed by grade I IVH. The study results showed fewer cases with grade III IVH and even fewer with grade IV. **Conclusions.** The lower the gestational age is, the higher the risk of developing IVH, being the most common cause of neonatal intracranial haemorrhage. Asphyxia at birth is one of the leading causes of early neonatal death.

**Keywords:** preterm infant, neurological complications, intraventricular haemorrhage

## Fetal heart analysis in the first trimester. New kid on the block

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**Introduction.** Prenatal evaluation of the heart and an early recognition of congenital heart disease are important for a timely intervention. **Objective.** The current paper challenges a convolutional neural network to address the computationally undebated task of recognizing the key elements from the first-trimester fetal heart scanning. **Methodology.** Frames depicting the views of interest were labeled by obstetricians and given to several deep learning (DL) architectures as a classification task against other irrelevant scan sights. Four key parameters were established: atrioventricular flows, aorta emergence, the crossing of the great vessels (X sign) and the arches confluence (V sign). DL methodology included data preprocessing, frame classification and experiments where the setup included six DL architectures that

were fine-tuned on the training frames. **Results.** The test yielded a 95% accuracy, with an F1-score ranging from 90.91% to 99.58% for the four key parameters. **Conclusions.** The potential in supporting heart scans, remain very important even from such an early fetal age, when the heart is still quite underdeveloped.

**Keywords:** fetal heart, ultrasound, first trimester pregnancy, deep learning, artificial intelligence, prenatal diagnosis

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## Retinopathy of prematurity: the importance of screening

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**Introduction.** Retinopathy of prematurity (ROP) represents a proliferation of the retinal blood vessels that occurs in low-birth weight (LBW) preterm newborns, especially as a consequence of oxygen therapy. This disorder is a severe prematurity complication, often with unfavorable evolution, leading to blindness in the absence of the treatment. The screening for retinopathy of prematurity has proven extremely important. In Romania, it is recommended to all preterm newborns with birth weight below 2000 g and/or gestational age below 34 weeks, leading to the detection of severe disorders and cecity prevention. Screening starts by 4-6 postnatal weeks and/or 32-34 weeks corrected age. The treatment modalities are laser therapy of the neoformation of vessels that occur in the peripheral retina or cryotherapy using a tube that destroys abnormal levels at the retina level. **Materials and method.** This retrospective study was done on a period of one year in the Preterm Clinic of the "Louis Țurcanu"

Emergency Clinical Hospital for Children, Timișoara, and included 80 preterm newborns with gestational age below 34 weeks and birth weight below 2000 g who suffered from different stages of retinopathy. **Results.** From a total of 902 admitted patients, 428 were included for screening (47%). Of these, 80 preterms (18.69%) developed retinopathy, and were distributed as follows: stage I – 49 (61.25%), stage II – 12 (15%), stage III – 8 (10%), stage IV – 11 (13.75%). Those from the fourth stage lot required laser therapy, 8 (72.72%) had a good recovery after surgery, 3 (27.27%) required reintervention, and one case (1.25%) had an unfavorable evolution that led to stage V ROP. **Conclusions.** An imperative need of following a strict screening pattern for retinopathy of prematurity is needed, leading to the prevention of a permanent and disabling disease.

**Keywords:** retinopathy, newborn, premature, screening

## Semilobar holoprosencephaly – a rare pathology in the clinical practice

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**Introduction.** Holoprosencephaly represents a complex birth defect, resulted from the incomplete prosencephalon separation during the 4<sup>th</sup> and the 6<sup>th</sup> weeks of gestation. There are four main subtypes: lobar, semilobar, alobar and middle interemispheric variant. Lobar holoprosencephaly is characterized by an interhemispheric fissure along almost the entire midline; the semilobar one is characterized by an incomplete forebrain division; in the alobar subtype, no hemisphere separation is seen, while in the middle variant, the frontal and parietal lobes separation is absent. **Objectives.** Reporting a rare case in the clinical practice, with an incidence of 1:250 products of conception and with poor prognosis. Highlighting the role of prenatal active care and interdisciplinary team in diagnosis and recovery. **Case report.** A newborn with semilobar holoprosencephaly associated with midline facial cleft, born to healthy parents, uncared pregnancy, with no periconceptional folic acid supplementation. The baby was born by vaginal delivery, at 36 weeks of gestation. Anthropometric measure-

ments: weight 2800 g, length 49 cm, head circumference 30 cm; Apgar score 4/5, requiring resuscitation. **Results.** Microcephaly (reduced neurocranium), hypotelorism and midline facial cleft were observed. After birth, generalized tonic-clonic seizures were discovered, evolving toward *status epilepticus* difficult to control with triple antiepileptic drug therapy. Subsequently, the newborn presented with multiple episodes of central origin fever. The aEEG showed ictal pattern. The MRI and CT scans described the absence of *septum pellucidum*, with fused midline lateral ventricles and thalami and focal absence of the anterior nasal septum, confirming the diagnosis. The progress of this case was unfavorable, with poor prognosis. **Conclusions.** The importance of prenatal screening is asserted together with neural tube defects prevention by folic acid supplementation during the preconceptional period and the first trimester of pregnancy.

**Keywords:** holoprosencephaly, cleft, birth defect, newborn

## Congenital diaphragmatic defects in neonates – diagnostic difficulty

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Diaphragmatic defects, such as diaphragmatic hernia and diaphragmatic eventration, affect neonates from the first hours of life. Diaphragmatic hernia is a developmental defect of the diaphragm that allows abdominal viscera to herniate into the chest. Unlike diaphragmatic hernia, diaphragmatic eventration is a rare condition, representing 5% of all diaphragmatic defects, which consists in the thoracic ascent of part or all of the diaphragmatic muscle, without a lack of continuity in the muscle. The congenital form is associated with high rates of neonatal morbidity and mortality, due to fetal pulmonary hypoplasia and the associated malformations. Ultrasonography and nuclear magnetic resonance are the best investigation techniques in the prenatal diagnosis of congenital diaphragmatic defects. Prenatal differentiation between congenital diaphragmatic eventration

and congenital diaphragmatic hernia can be important but difficult, due to subtle ultrasonographic discoveries and the great similarity between them. Newborns with large diaphragmatic defects (hernia or eventration), who show symptoms, need supportive treatment and surgical correction of the defect. Excluding the diagnosis of diaphragmatic hernia does not exclude the need for surgery, but helps the surgeon in establishing the surgical approach. The prognosis is influenced by the clinical and paraclinical evolution, the degree of pulmonary hypoplasia and the presence of other abnormalities. Although both diaphragmatic defects have the same effects on lung development, diaphragmatic eventration has a better prognosis.

**Keywords:** congenital diaphragmatic eventration, newborn, differential diagnosis

## Impact of maternal inflammation on preterm newborns

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**Introduction.** Preterm birth is an important cause of mortality and morbidity in neonatology. It induces a number of acute disorders, as well as chronic diseases, with long-term effects on the newborn. About 70% of all preterm births are spontaneous, being caused by the premature rupture of membranes or by preterm labor. In half of the cases of preterm labor, inflammatory syndrome or sustained inflammation is associated. This inflammatory process will have an effect on the organs and systems of the neonate. **Effects of inflammation on newborns.** Labor occurs under proinflammatory conditions, with the involvement of cytokines. Chemotactic activity and cytokine production are different in the case of premature rupture of membranes, compared to the normal rupture of membranes. Inflammatory mediators will reach the fetus through the amniotic fluid or by vertical transmission through the umbilical cord and will act on the neonatal organs. Effect of inflammation on the lungs: the high maternal cytokine level will increase the risk of bronchopulmonary dysplasia in the newborn. Inflammatory mediators affect the regulation of angiogenesis, morphogenesis and cell growth in the lungs. Studies have highlighted a correlation between microbiota and immunity – i.e., the presence of a lung-intestine axis regarding mucosal status. Effect on the heart: cytokine

release is correlated with the development of pulmonary hypertension, which will affect the right ventricle and will induce systolic and diastolic dysfunction. Hyperoxia caused by inflammation will have an effect on left ventricular structure and contractility. Effect on the intestine: cyclooxygenase and platelet activating factors play a role in the inflammatory pathogenesis of NEC. The major consequence at the intestinal level of maternal chorioamnionitis, chronic ischemia during pregnancy and antibiotic exposure is represented by necrotizing enterocolitis. Effect on the central nervous system: fetal inflammation, as well as neonatal inflammation caused by infections may generate effects on the brain, inducing white matter lesions, determining periventricular leukomalacia that will evolve with cerebral palsy. The high levels of IL-1 $\beta$ , IL-6 and especially TNF- $\alpha$  will have a toxic effect on developing oligodendrocytes, as well as on neurons. The imbalance of the intestine-brain axis plays an important role in the neurocognitive development. **Conclusions.** Inflammation during pregnancy has effects on the fetus and, subsequently, on the newborn. Inflammatory mediators in the amniotic fluid induce lesions in the lungs, central nervous system, as well as in other organs.

**Keywords:** preterm birth, inflammation, neonatal effect of inflammation

## The clinical progression of a newborn from a mother with HBP and HIV-positive – case study

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Maternal HIV infection and related comorbidities may have two outstanding consequences to fetal health: mother-to-child transmission and adverse perinatal outcomes, such as the potential risk of preterm delivery and intrauterine fetal growth restriction (IUGR). Furthermore, the HIV infection may induce or worsen a preexistent high blood pressure (HBP), which is an additional risk for the aforementioned conditions. Our case presentation is represented by a preterm newborn (35 weeks) with maternal history of chronic HBP and

HIV infection discovered in pregnancy, which led to IUGR and premature birth of the fetus due to the fetal distress. The peculiarity of the case is represented by the presence of meconium-stained amniotic fluid in a late preterm newborn. Moreover, the newborn presents in the clinical evolution a high risk of developing bronchopulmonary dysplasia.

**Keywords:** high blood pressure, HIV infection, intra-uterine fetal growth restriction, meconium-stained amniotic fluid

## Diagnosis difficulties in a suspected case of Zellweger syndrome

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**Introduction.** Zellweger syndrome is a rare congenital disease, characterized by the reduction or absence of peroxisomes in the cells. The evolution is severe, resulting in death within the first year of life. **Objective.** Presentation of a particular case with multiorgan failure, in which the diagnosis of Zellweger syndrome was discussed. **Case presentation.** A full-term newborn was hospitalized at the age of 17 days for dyspnea, capricious appetite, cyanosis, desaturation, affirmatively with sudden onset; from dispensary pregnancy – GIII, PII. From the hereditary collateral antecedents, we notice an ended pregnancy and a newborn died at 3 weeks of age. Evolutionarily, the newborn presented acute respiratory distress syndrome, requiring respiratory support, anuria, absence of intestinal transit, marked hypotonia, capping of the eyes, generalized edema, and purple elements. **Results.** Biological: altered coagulogram, increased transaminases, severe hyperkalemia, increased renal tests, severe metabolic acidosis refractory to

treatment, severe hypoglycemia, increased ferritin. Echocardiography detected DSA, mitral and tricuspid insufficiency. The abdominal radiography with contrast substance refuted the suspicion of a surgical pathology or a digestive malformation. The genetic consult raised the suspicion of Zellweger syndrome and the additional genetic investigations were also performed for metabolic diseases. The evolution was unfavorable, with death due to multiorgan failure. **Conclusions.** Metabolic diseases are an important chapter in neonatal pathology. The diversity of clinical manifestations makes them difficult to recognize and diagnose, sometimes with an unfavorable prognosis of the disease. In the presented case, considering the heredocollateral antecedents, the importance of genetic and metabolic investigations is noted, for the confirmation or refutation of a genetically transmissible disease, as well as of the genetic counseling.

**Keywords:** Zellweger syndrome, newborn, multiorgan damage



## CMV transmission through breastfeeding

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Cytomegalovirus (CMV) infection is a highly debated topic worldwide, as CMV is a virus that causes infections all throughout one's life. The virus is contracted by the newborn through breast milk and may cause severe illnesses, with a heavy symptomatology in premature neonates. However, for term newborns, the perinatal infection with CMV may occur free of consequences. Almost all CMV-positive mothers eliminate the virus through the milk. Even though breast milk is the best source of nutrients – especially for

preterm neonates –, it is sometimes not the safest option when considering the possibility of viral shedding through the milk. The current methods to expel the virus from the milk are pasteurization, freezing, ultraviolet C, or microwave irradiation. These have different levels of efficacy and effects on breast milk, and thus further studies for clearer evidence are still needed.

**Keywords:** CMV, breastfeeding, breast milk, premature newborn

## Potential new predictive risk factors for retinopathy of prematurity – where are we now?

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Retinopathy of prematurity (ROP) is still a serious morbidity, affecting the future quality of life, as it may end in blindness if is not correctly and in a timely manner detected and treated. Several risk factors are already well known: severe prematurity, intrauterine growth restriction, aggressive oxygen therapy, repeated blood transfusions, sepsis, necrotising enterocolitis (controversies), poor nutrition and poor weight gain. Based on this knowledge, there were elaborated guidelines for ROP screening, worldwide recommended. Recently, there have been large discussions about other potentially associated risk factors, such as maternal diabetes, several hematologic parameters, especially thrombocytes. The association of thrombocytopenia in small-for-gestational-age (SGA) infants may be a better predictor for ROP, but more studies are needed in order to confirm it. Although anaemia during the first week was a significant risk factor for severe ROP, requiring treatment among infants born below 28 weeks of gestation, elevated erythropoietin serum levels were not associated with severe ROP. The replacement of fetal hemoglobin (HbF) during transfusion with adult Hb may explain the higher risk for ROP, while maintaining a higher HbF may protect against ROP. Platelet mass index was supposed to be a more reliable risk factor for developing ROP and it might represent a

useful orientation tool for prioritising screening. There are studies demonstrating that maternal diabetes, preeclampsia and eclampsia were protective factors, except for type 1 ROP. The role of vascular endothelial growth factor (VEGF) in the development of ROP was demonstrated, but serum concentrations are high only in the first phase of ROP. Severe lung impairment, like in pneumonia, respiratory distress syndrome by surfactant deficiency or severe chronic lung disease, was found to be well related with severe stages of ROP. Recently, in a multivariable analysis, statistically significant perinatal risk factors for severe ROP were: lower birth weight, younger gestational age, male sex, Hispanic ethnicity, race versus black race, outborn delivery, intubation and mechanical ventilation at delivery room. Studies reported an independent association between hyperglycaemia in the first postnatal week and the later development of treatment-demanding ROP, when adjusted for known risk factors. Further research is needed to confirm if the use of inotropes, intraventricular haemorrhage, *in vitro* fertilization, and multiple pregnancies may be considered as reliable risk factors for developing ROP in very premature infants.

**Keywords:** retinopathy of prematurity, newborn, blood transfusions, platelet mass index, thrombocytopenia, VEGF

## Vertical transmission of SARS-CoV-2 and outcomes of neonates born to mothers with COVID-19

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**Introduction.** First appeared in Wuhan, China, at the end of 2019, COVID-19 is an infectious disease caused by SARS-CoV-2, a virus belonging to *Coronaviridae* family. It generated a pandemic spread, as the disease is human-to-human and ambient transmissible, infecting all age categories. People with comorbidities represent the most vulnerable population, leading to a potentially severe and fatal evolution. Pregnancy represents a high-risk situation if infection occurs. Furthermore, any prenatal pathologies or such appeared during pregnancy lead to an even higher chance of complications and severity. This study aims to elaborate several answers to the frequently asked question on if, when and how can mother-to-fetus transmission affect the pregnancy and its outcome. **Materials and method.** This report represents a summary of the main literature references regarding virology, clinical, paraclinical data, pregnancy diagnosis and results, along with probable ways of viral mother-to-fetus transmission. **Results.** Even though the number of bibliographic refer-

ences is high and increasing, there is still little evidence regarding vertical transmission and most of it refers to extremely severe disease cases. Nearly all appeared during the last trimester of pregnancy. This aspect is reflected in the statistical data and illustrates that, no matter the way of transmission, the number of infected newborns is low compared to the pandemic dimensions. A meta-analysis done by X.L. Goh, Y.F. Low, et al., including 17 studies, describes 9 positive newborns out of 330 births to positive mothers. **Conclusions.** Further research that can sustain or deny the viral mother-to-fetus transmission at the uterine-placental interface is necessary. Actual immunologic data are incisive and show that the placenta is an important barrier that protects the fetus against this kind of infection. Many pathological conditions can disturb placental circulation and can create the possibility of fetal compromise.

**Keywords:** newborn, SARS-CoV-2, COVID-19, pregnancy, vertical transmission

## Can corticosteroid therapy influence the management and prognosis of intractable seizures in newborns in view of reducing inflammation and improving eurodevelopmental outcome?

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Neonatal seizures are one of the main medical emergencies, with increased variability in terms of etiology, clinical manifestations, electroencephalographic modifications and brain imaging. In some cases, patients have a refractory response to anticonvulsant therapy, compared to other age groups for whom it has increased efficiency. Research is in progress in order to elucidate the pathophysiological mechanisms of neonatal sei-

zures, depending on the etiology, thus new therapeutic methods are applied to nonresponsive cases. New directions in literature and medicine studies take into consideration the possible influence of corticosteroid therapy for long-term neurodevelopmental outcome in these patients.

**Keywords:** neonatal seizures, corticosteroid therapy, neuroinflammation, neurodevelopment

## Congenital rubella and syphilis coinfection

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Rubella is a self-limiting viral infection in children and adults, but with major effects on the fetus if the virus is contracted by the seronegative pregnant woman. Syphilis is a sexually transmitted infection caused by *Treponema pallidum*, and pregnant women with untreated or inadequately treated syphilis can transmit the disease through transplacental passage to the fetus or at the birth of the newborn. We present the case of two newborns from uninvestigated pregnancies with concomitant infection with both rubella and syphilis.

In both cases, the clinical manifestations, as well as the laboratory changes were similar. The clinical signs have been present since birth, with newborns requiring care in the neonatal intensive care unit. The association of two congenital infections with important effects on the fetus and newborn is quite rare. Although there are infections that can be prevented or treated, the pregnant woman's lack of addressability to the medical system can have serious consequences for the newborn.

**Keywords:** rubella, syphilis, congenital, coinfection

## Particularities of the newborns with fetal growth restriction in neonatal intensive care units

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Infants with fetal growth restriction (FGR) who did not achieve full *in utero* growth potential due to genetic or environmental factors are at an increased risk for a significant morbidity and mortality compared with infants with normal *in utero* growth. The definition and the management of this pathology have to be guided by a serial ultrasonographic evaluation in which a corroborated dynamics of numerous parameters must be analyzed: Doppler studies about the maternal dimension (uterine arteries) and the fetal one (umbilical artery, middle cerebral artery, venous duct, aortic isthmus, umbilical vein), biometrics and fetal biophysical score. The timing of placental insufficiency, the severity of the FGR, the degree of cardiovascular adaptation and the gestational age are critical factors that change the prognosis of these newborns. In the neonatal period, newborns with FGR show early signs of cardiac, vascular, pulmonary and

rheological deficits and require admission to neonatal intensive care units. The diagnosis of newborns with FGR can be established antenatally by ultrasonographic evaluation, which confirms the fetal biometric measurements with gestational age, or at birth, when less than the 10<sup>th</sup> percentile weight is found. Neonatal complications associated with FGR include prematurity, perinatal asphyxia, deficient thermoregulation, hypoglycemia, polycythemia and immune deficiencies. Newborns with FGR need special attention regarding nutrition, considering that they are disadvantaged by the digestive immaturity and the reduced diversity of the digestive tube microbioma. The present research brings into discussion a global analysis of the newborn with FGR, highlighting the nutritional particularities of this category.

**Keywords:** intrauterine growth restriction, antenatal diagnostic, neonatal complications

## Neonatal hepatitis associated with plurimalformative syndrome, ascites fluid and LLA suspicion

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**Introduction.** Idiopathic neonatal hepatitis affects 1:2500 live births. In 80% of cases, the causes cannot be identified, but they can be classified into: viral infections caused by cytomegalovirus, rubella or A, B or C hepatitis viruses, metabolic problems due to liver immaturity, giant-cell idiopathic hepatitis.

**Objectives.** The authors aim to present the difficulties that a diagnosis poses in a case of neonatal hepatitis associated with ascites and plurimalformative syndrome. **Case presentation.** We introduce the case of a newborn, aged 2 weeks, hospitalized in our clinic, showing cholestatic jaundice, thrombocytopenia and ascites. The newborn comes from a monitored pregnancy, the mother being known with thrombophilia, GIV, PIII, natural birth, GA=37 weeks, BW=3000 g and AI=5/6, requiring resuscitation maneuvers in the birth room. The newborn was diagnosed intrauterinely with plurimalformative syndrome and suspected Down syndrome. Under the hematology evaluation, the diagnosis of acute leukemia was refuted. Clinically, the newborn

shows oblique eyelid slits, lower inserted ears, malformed lower limbs, intense volume-relaxed abdomen, collateral flow present, and intensely jaundiced skin.

**Results.** Biologically, the newborn presents persistent thrombocytopenia, anemic syndrome, conjugated hyperbilirubinemia, and elevated values of transaminases. Tests results for TORCH syndrome and viral hepatitis were negative, and central and peripheral cultures turned back sterile. The genetic consultation confirmed the diagnosis of trisomy 21 by Robertsonian translocation. Considering the malformative pathology, the evolution was unfavorable. **Conclusions.** Malformative syndromes associated with severe pathologies – in our case, hepatitis associated with ascites – generally have a poor prognosis. Cholestasis in the neonatal period is difficult to diagnose, requiring a complete anamnestic evaluation correlated with laboratory investigations, molecular biology and genetic studies.

**Keywords:** neonatal hepatitis, ascites, cholestatic jaundice

## Postnatal management of the newborn with congenital diaphragmatic hernia

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Diaphragmatic hernia is a congenital malformation of multifactorial etiology, characterized by a structural defect of the diaphragm, which may result in abdominal viscera ascension into the thoracic cavity. The incidence of the disease varies between 1:2000 and 1:5000 births. The diagnosis is divided into antenatal and postnatal components. An important role in the increase of the antenatal diagnosis rate is attributed to the obstetric ultrasound from the 16<sup>th</sup> week of age, the presence of polyhydramnios being a negative prognosis element. The postnatal diagnosis can raise the suspicion of diaphragmatic hernia based on clinical signs from the delivery room, which must be confirmed by chest X-ray and cardiac and abdominal ultrasound. The main aim is to stabilize the newborn

and correct the oxygenation and blood pressure; it is possible to opt for the conventional ventilator or high-frequency oscillatory ventilation, while maintaining the low inspiratory pressure to avoid barotrauma. Depending on the case, vasodilator or surfactant medication may be required. Congenital diaphragmatic hernia has both acute and late complications. One of the most frequent acute complications is persistent pulmonary hypertension, while long-term ones may even include neurological sequelae. The survival rate has improved, reaching 70-90%, depending on the particular characteristics for each case.

**Keywords:** congenital diaphragmatic hernia, postnatal management, intensive care, ventilation, preoperative care

## Prevention and treatment strategies in necrotizing enterocolitis

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Necrotizing enterocolitis (NEC) is a life-threatening illness, almost exclusively affecting neonates. Its prevention begins in the prenatal period, with a correct management of pregnancy and the prevention of prematurity. T.V. Santulli highlighted, since 1974, in his review, three factors involved in the etiology: local factors, bacteria and diet, but he emphasizing the role of stress in the increased incidence of perinatal complications. This paper aims to present the involvement of pathophysiological mechanisms in the new preventive and therapeutic strategies of NEC, along with the presentation of the experience of the Neonatology Clinic I, Cluj-Napoca. The definition has been continuously updated,

with the deepening of the etiopathogenesis. The concept of microbiome and its involvement in the pathology of the individual contributed to the understanding of the prevention mechanisms offered by the mother milk. The specific management of these premature infants is complex, with clinical trials supporting or abandoning some therapies over time. The experience of the Neonatology Clinic I supports breastfeeding as a protective factor against NEC and reveals, once again, the involvement of perinatal asphyxia and stress in increasing the risk of premature newborn for this pathology.

**Keywords:** premature newborn, NEC, risk factors, protective conditions

## Congenital anomalies of the lower urinary tract

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Congenital anomalies of the lower urinary tract (CALUTs) are some of the most common birth defects in newborns, representing approximately 20% to 30% of all anomalies identified in the prenatal period during routine antenatal ultrasonography. CALUTs include a broad spectrum of structural and functional abnormalities of the collecting system, bladder, and urethral abnormalities. It occurs in isolated form, but can be a part of a genetic syndrome, a chromosomal disorder, or an inborn error of metabolism involving other body systems. Studies indicate monogenic causes for some of these diseases in which implicated genes can encode smooth muscle, neural or urothelial molecules, or transcription factors that regulate their expression. Epigenetic alternations, such as DNA methylation, may profoundly affect the expression of renal genes, such mechanisms being implicated in gene expression of aging human kidneys. There is preliminary evidence that similar mechanisms may be operative in human renal malformations. Secondarily, non-genetic changes might themselves perturb the normal trajectory of organogenesis, due to alterations in maternal diet or the presence of maternal disease. Diabetes is accepted as one of the risk factors for congenital anomalies generally. Increased risk of CALUT is associated with any form of diabetes in pregnancy compared with nondiabetic pregnancies. Prevalence of CALUT: bladder extrophy – 0.002% births, megabladder – 0.30-0.06% in the first trimester, posterior urethral valve – 0.01% of births, primary non-syndromic vesicoureteric reflux – 1-10% in young children, Prune-Belly syndrome – 0.004% of births, ureteropel-

vic junction obstruction – up to 0.04% of newborns, urofacial syndrome – the prevalence is unknown, but there were around 150 postnatal cases reported. CALUTs often have poor birth outcomes owing to the limited experience of physicians in developing countries regarding antenatal and postnatal diagnosis. Some patients are diagnosed antenatally during anomaly scan which examines the kidney, outflow tracts, and the amniotic fluid volume, while others remain asymptomatic till adolescence. Antenatal ultrasounds correctly diagnose CALUT in 60-85% of infants, especially if imaging is performed in the third trimester. Infants with bilateral and severe CALUT have significant renal compromise at birth. Recent advances in the early diagnosis of fetal CALUT, with an increase in fetal surgical interventions, have led to a growing number of neonatal survivors born with severe renal dysfunction. The early multimodal management includes neonatal surgical interventions directed toward establishing adequate urine flow, respiratory support with the assessment of pulmonary hypoplasia, and establishing metabolic control to avoid the need for dialysis intervention. Over half of pregnancies involving severe CALUTs have adverse birth outcomes, such as stillbirth or even spontaneous abortion. CALUTs have severe implications for the health system, as they can be responsible for up to 50% of pediatric chronic kidney disease cases. CALUT is one of the major underlying diseases in the young adult population on renal replacement therapy.

**Keywords:** newborn, antenatal diagnosis, urinary tract congenital malformations, birth defects

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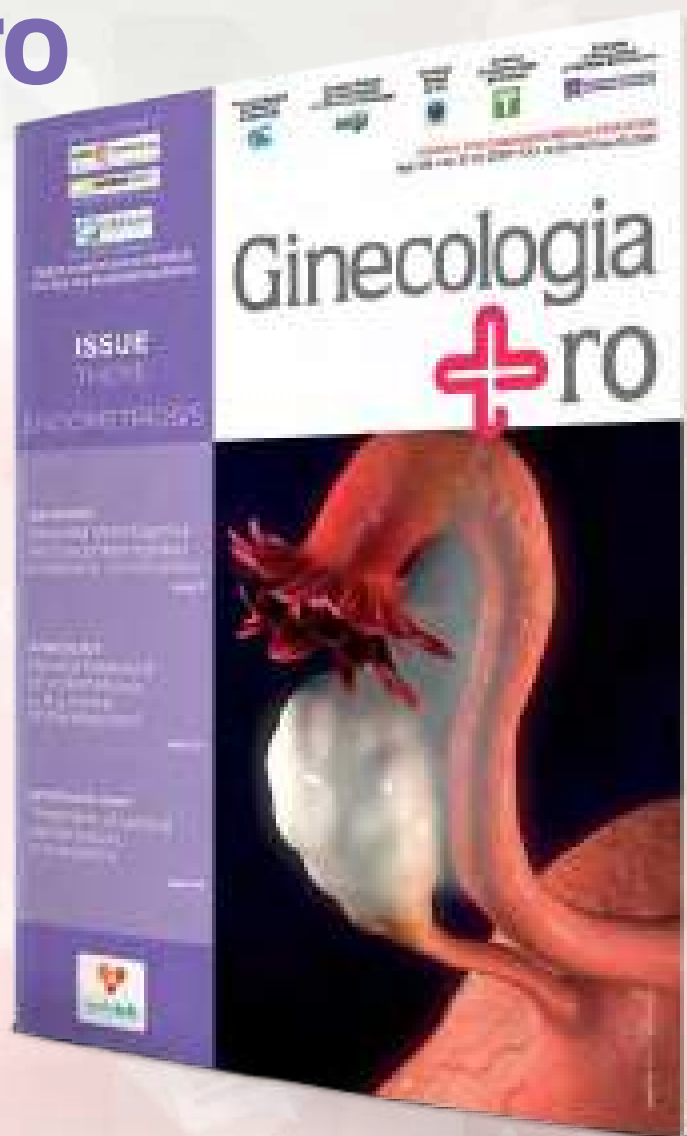
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