



November 19-21, 2020

# Congress Program & Abstract Book

# Timetable

## THURSDAY, NOVEMBER 19, 2020

	HALL I	HALL II
13:30-13:35	PRE-CONGRESS WELCOME	14:00-16:45 LASER COURSE See page 100
13:35-14:20	THE BEST OF RBMO 2019-2020	
14:20-15:20	INDUSTRY SUPPORTED SESSION See page 101	
15:20-15:50	INDUSTRY SUPPORTED SESSION See page 101	
15:50-16:50	OPENING SESSION NOBEL PRIZE LAUREATE ROBERT G. EDWARDS ANNUAL LECTURE BEST ABSTRACT AWARDS ANNOUNCEMENT	
17:00-18:05	PLENARY SESSION	

## FRIDAY, NOVEMBER 20, 2020

	HALL I	HALL II	HALL III
	INFERTILITY/ART/IVF	GYNECOLOGY	FETOMATERNAL MEDICINE
09:00-10:30	FAILURE OF IVF – WHAT TO CHECK, WHAT TO TRY	CONTRACEPTION: THE UNDER-APPRECIATED BENEFITS	PRENATAL DIAGNOSIS
10:30-11:00	Visit the virtual exhibition and e-poster hall		
11:00-12:30	DIAGNOSTIC PROCEDURE	ADVANCES IN HORMONAL AND NON-HORMONAL RESEARCH	PERIPARTUM COMPLICATIONS
12:30-15:05	Visit the virtual exhibition, e-poster hall and early afternoon sessions		
12:30-14:00	12:30-13:30 INDUSTRY SUPPORTED SESSION See page 102	NON-ABLATIVE AND MICRO-ABLATIVE LASERS IN GYNECOLOGY	FERTILITY PRESERVATION (part of the Infertility/ART/IVF track)
14:00-14:05	Break		
14:05-15:05	ISMAAR SESSION: THE ROLE OF ULTRASOUND IN IVF PROGRAM	INDUSTRY SUPPORTED SESSION See page 102	GLOBAL AND WOMEN'S HEALTH
15:05-15:10	Break		
15:10-16:40	PROGESTERONE AND ESTROGENS: WHAT TO KNOW FOR PMA FOR OPTIMIZING RESULTS A PREIS SCHOOL ACADEMY SESSION	VULVAR PAIN AND CO-MORBIDITIES	GESTATIONAL DIABETES MELLITUS (GDM)
16:40-17:00	Visit the virtual exhibition and e-poster hall		
17:00-18:30	ADVANCED SOLUTIONS TO IMPROVE FERTILITY	HPV	HIGH RISK PREGNANCY

## SATURDAY, NOVEMBER 21, 2020

	HALL I	HALL II	HALL III
	INFERTILITY/ART/IVF	GYNECOLOGY	FETOMATERNAL MEDICINE
09:00-10:30	RESEARCH	OVARIAN CANCER – NEW INSIGHTS AND CURRENT TREATMENT STANDARDS	GENERAL HEALTH AND FERTILITY
10:30-11:00	Visit the virtual exhibition and e-poster hall		
11:00-12:30	ADD-ONS LABORATORIES AND CLINICAL PROCEDURES	RECENT ADVANCES ON POI AND LINK WITH DNA REPAIR/CANCER GENES	ROUND TABLE DISCUSSION ON PRETERM LABOR
12:30-15:05	Visit the virtual exhibition, e-poster hall and early afternoon sessions		
12:30-14:00	WORKSHOP ON UNDERSTANDING CURRENT ADD-ONS	PCOS AT MENOPAUSE	CAESAREAN SECTION AND DELIVERY
14:00-14:05	Break		
14:05-15:05	INDUSTRY SUPPORTED SESSION See page 103	ISMAAR SESSION: MILD IVF	ULTRASOUND IN PREGNANCY
15:05-15:10	Break		
15:10-16:40	PGT-A: HELPFUL OR HARMFUL?	ENDOMETRIOSIS	PRE-ECLAMPSIA TOXEMIA (PET) AND INTRAUTERINE GROWTH RETARDATION (IUGR)
16:40-17:00	Visit the virtual exhibition and e-poster hall		
17:00-18:30	PCOS	SLS: THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS	INTRAPARTUM MONITORING

\*All times are according to Central European Time (CET)

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## *Words of Welcome from COGI Chairpersons*

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### **Dear Colleagues,**

COGI and RBMO are delighted to welcome you to the 28th World Congress on Controversies in Obstetrics, Gynecology and Infertility (COGI) taking place online from November 19-21, 2020.

World renowned leaders in the field of Ob/Gyn and infertility, will review advances, breakthroughs and controversies in the field via round table discussions, debates, and lectures. Highlights will include the "Robert G. Edwards Nobel Prize Laureate" lecture, cutting edge "countercurrent" lectures by leading experts "who think differently", an inspiring fetomaternal medicine program, sessions on early prenatal diagnosis, pregnancy support, age-related risks, nutrition, the epidemic of multiple pregnancies, HPV, menopause, and more. In addition, the voice of the next generation of physicians, scientists and researchers will be heard as part of the Young Scientist Competition which will be presented as e-Posters.

We would like to thank our industry supporters for their investment in COGI. Without this continued support, we would not be able to offer such a high level of knowledge to be shared with a truly international delegation. We look forward to thought-provoking debates, enjoyable discussions and an overall exchange of knowledge.

We wish you an excellent congress experience.

We hope to welcome you in person in 2021, as the COGI experience will continue.

Sincerely,

### **COGI Congress Co-Chairpersons**



**Zion Ben Rafael**  
*Israel*



**Bart C.J.M. Fauser**  
*Netherlands*



**Rene Frydman**  
*France*

# General Information

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## VENUE

Online

## LANGUAGE

The official language of the congress is English.

## COGI ONLINE PLATFORM HOURS

Thursday, November 19 13:00-18:30

Friday, November 20 08:30-18:30

Saturday, November 21 08:30-18:30

## CONGRESS ADMISSION

Admission to the scientific sessions, exhibition area and e-Posters is available to registered delegates only.

## EXHIBITION OPENING HOURS

Thursday, November 19 13:00-18:30

Friday, November 20 08:30-18:30

Saturday, November 21 08:30-18:30

## POSTERS

All the posters are presented in electronic format. The e-Posters are in a digital hall on the platform.

## CERTIFICATE OF ATTENDANCE (non-CME/CPD)

Certificates of attendance will be sent by email after the congress to all registered delegates.

## CME ACCREDITATION

The 28<sup>th</sup> COGI Congress has been accredited by the European Accreditation Council for Continued Medical Education (EACCME®) for a maximum of 18 CME credits (ECMEC®s).

To receive your CME accreditation certificate, please visit the congress website after the congress and complete the online form. Your certificate will be sent to you approximately 60 days after completion of the survey.

## LIABILITY AND INSURANCE

The COGI Congress secretariat and the organizers cannot accept liability for personal accidents, or loss or damage to private property of participants, either during or directly arising from the 28<sup>th</sup> COGI Congress.

## RECORDING POLICY

Recording (photographic, video and audio) of the session is **strictly prohibited**. A recorded version of the congress will be available on a password protected website for 3 months after the congress. The link and password will be sent to registered delegates after the congress.

## SOCIAL MEDIA

Follow COGI social media pages for the latest updates, key date reminders, and discussions with colleagues and experts from around the world.

Facebook: **COGI Congress**

LinkedIn: **Controversies in Obstetrics, Gynecology & Infertility (COGI)**

Twitter: **@cogicongress / #COGI**

Youtube: **cogicongress**

Instagram: **cogi\_congress**





# know what matters in



**Women's  
and Children's  
Health**

[karger.com/childrenshealth](https://karger.com/childrenshealth)



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*Scientific Program*

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## THURSDAY, NOVEMBER 19, 2020

### PLENARY SESSIONS – HALL I

<b>13:30-13:35</b>	<b>PRE-CONGRESS WELCOME</b>	<b>LOBBY</b>
Chairpersons	<b>Zion Ben Rafael, Israel</b> <b>Bart Fauser, Netherlands</b>	
13:30-13:35	Welcome to COGI	
<b>13:35-14:20</b>	<b>THE BEST OF RBMO 2019-2020</b>	<b>HALL I</b>
Capsule	The three best papers published in RBMO in 2019 are presented in this session.	
Chairperson	<b>Bart Fauser, Netherlands</b>	
13:35-13:50	Does presence of adenomyosis affect reproductive outcome in IVF cycles? A retrospective analysis of 973 patients <b>Sunita Sharma, India</b>	
13:50-14:05	Do men with normal testosterone-oestradiol ratios benefit from letrozole for the treatment of male infertility? <b>Liu Shuling, Singapore</b>	
14:05-14:20	When only one embryo is available, is it better to transfer on day 3 or to grow on? <b>Joyce S. Xiao, Australia</b>	
<b>14:20-15:20</b>	<b>INDUSTRY SUPPORTED SESSION</b> See page 101	<b>HALL I</b>
<b>15:20-15:50</b>	<b>INDUSTRY SUPPORTED SESSION</b> See page 101	<b>HALL I</b>
<b>15:50-16:50</b>	<b>OPENING SESSION</b>	<b>HALL I</b>
Chairpersons	<b>Zion Ben Rafael, Israel</b> <b>Bart Fauser, Netherlands</b> <b>Wolfgang Henrich, Germany</b>	
15:50-16:35	Nobel prize laureate Robert G. Edwards annual lecture: Persistent infections in the early period of life as risk factors for diseases decades later on By Nobel prize laureate <b>Harald zur Hausen, Germany</b>	
16:35-16:40	Welcome from <b>Jens Spahn, Minister of Health, Germany</b>	
16:40-16:50	Best Abstract Award Announcement	
<b>16:50-17:00</b>	<b>Break</b>	
<b>17:00-18:05</b>	<b>PLENARY SESSION</b>	<b>HALL I</b>
Chairpersons	<b>Bart Fauser, Netherlands</b> <b>Wolfgang Henrich, Germany</b> <b>Georg Griesinger, Germany</b>	
17:00-17:20	Why doesn't the ovary benefit from the 'longevity dividend'? <b>Gerald Schatten, USA</b>	
17:20-17:40	Gut brain: Its role in women's health <b>Vincenzo Stanghellini, Italy</b>	
17:40-18:05	Developmental potential of aneuploid human embryos cultured beyond implantation <b>Magdalena Zernicka-Goetz, UK</b> <b>Bailey Weatherbee, UK</b>	

### LASER COURSE - HALL II

<b>14:00-17:00</b>	<b>LASER COURSE</b> See page 100	<b>HALL II</b>
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## FRIDAY, NOVEMBER 20, 2020

### INFERTILITY/ART/IVF – HALL I

09:00-10:30	FAILURE OF IVF - WHAT TO CHECK, WHAT TO TRY	HALL I
Chairpersons	<b>Rene Frydman</b> , <i>France</i> <b>Georg Griesinger</b> , <i>Germany</i>	
09:00-09:20	Mitochondria and oocyte aging <b>Juan García Velasco</b> , <i>Spain</i>	
09:20-10:05 09:20 09:35 09:50	Debate: <b>Duo-stimulation</b> Pro: <b>Filippo Maria Ubaldi</b> , <i>Italy</i> Con: <b>Bart Fauser</b> , <i>Netherlands</i> Discussion	
10:05-10:30	The effect of ovarian stimulation on embryo ploidy status <b>Willem Verpoest</b> , <i>Belgium</i>	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	DIAGNOSTIC PROCEDURE	HALL I
Chairperson	<b>Ben Mol</b> , <i>Australia</i>	
11:00-11:20	Fertility enhancement using oil-and water-based contrast media with ultrasound guidance <b>Emmeline Lee</b> , <i>Australia</i>	
11:20-11:40	Tubal flushing with oil-based contrast should be offered to every infertile couple <b>Ben Mol</b> , <i>Australia</i>	
11:40-11:55	How far should we evaluate the couple's genetic risk? <b>Rita Vassena</b> , <i>Spain</i>	
11:55-12:10	Unexplained infertility: What do we do? <b>Fulco van der Veen</b> , <i>Netherlands</i>	
12:10-12:30	Special countercurrent lecture: The microbiome at ART <b>Joop Laven</b> , <i>Netherlands</i>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions

12:30-13:30	INDUSTRY SUPPORTED SESSION See page 102	HALL I
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#### 13:30-14:05 Break

14:05-15:05	ISMAAR SESSION: THE ROLE OF ULTRASOUND IN IVF PROGRAM	HALL I
Chairperson	<b>Rene Frydman</b> , <i>France</i>	
14:05-14:35	The role of advanced ultrasound to optimise IVF outcomes <b>Stuart Campbell</b> , <i>UK</i>	
14:35-15:05	How targeted ultrasound can help reduce complications and hospital admissions in the post COVID era <b>Geeta Nargund</b> , <i>UK</i>	

#### 15:05-15:10 Break



15:10-16:40	PROGESTERONE AND ESTROGENS: WHAT TO KNOW FOR PMA FOR OPTIMIZING RESULTS A PREIS SCHOOL ACADEMY SESSION	HALL I
Chairpersons	<b>Rene Frydman</b> , <i>France</i> <b>Gian Carlo Di Renzo</b> , <i>Italy</i>	
15:10-15:15	Introduction <b>Gian Carlo Di Renzo</b> , <i>Italy</i>	
15:15-15:35	Pharmacodynamics: What to know <b>Paul Piette</b> , <i>Belgium</i>	
15:35-15:55	Progesterone in fetal and neonatal brain protection <b>Michael Schumacher</b> , <i>France</i>	
15:55-16:15	Optimal vaginal progesterone use in assisted reproductive technology <b>Elena Labarta</b> , <i>Spain</i>	
16:15-16:35	Choice of protocols for progestogen usage in threatened miscarriage and recurrent pregnancy loss <b>Klaus Diedrich</b> , <i>Germany</i>	
16:35-16:40	Discussion Q&A	

**16:40-17:00 Virtual exhibition and e-poster viewing**

17:00-18:30	ADVANCED SOLUTIONS TO IMPROVE FERTILITY	HALL I
Chairperson	<b>Edgardo Somigliana</b> , <i>Italy</i>	
17:00-17:20	Kiss-peptin: Promise becomes the standard? <b>Cornelis B. Lambalk</b> , <i>Netherlands</i>	
17:20-17:40	Meiosis gene dysfunction as a cause of infertility <b>Willem Verpoest</b> , <i>Belgium</i>	
17:40-18:00	Luteal phase support: Balancing effectiveness and safety <b>Peter Platteau</b> , <i>Belgium</i>	
18:00-18:30	<b>Debate: Cesarean scar defect: When residual myometrial thickness is less than 3mm</b>	
18:00	Pro hysteroscopy: <b>Sylvia Mechsner</b> , <i>Germany</i>	
18:10	Pro laparoscopy: <b>Olivier Donnez</b> , <i>Belgium</i>	
18:20	Discussion	

## SATURDAY, NOVEMBER 21, 2020

### INFERTILITY/ART/IVF – HALL I

09:00-10:30	RESEARCH	HALL I
Capsule	Much of the published medical research is apparently flawed, cannot be replicated and/or has limited or no utility (Altman 1994).	
Chairperson	<b>Cornelis B. Lambalk</b> , <i>Netherlands</i>	
09:00-09:20	Are we neglecting scientific fraud? <b>Ben Mol</b> , <i>Australia</i>	
09:20-09:45	Repeated Implantation Failure (RIF): A misleading non-standardized definition that affects the quality of publication <b>Zion Ben Rafael</b> , <i>Israel</i>	
09:45-10:10	RCT's have a central role in medical research <b>Ben Mol</b> , <i>Australia</i>	
10:10-10:30	Big data is an important way forward in medical research. How can big data supplement RCT's? <b>Bart Fauser</b> , <i>Netherlands</i>	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	ADD-ONS LABORATORIES AND CLINICAL PROCEDURES	HALL I
Chairpersons	<b>Laura Rienzi</b> , <i>Italy</i> <b>Zion Ben Rafael</b> , <i>Israel</i> <b>Bart Fauser</b> , <i>Netherlands</i>	
Discussants	<b>Simon Fishel</b> , <i>UK</i> <b>Rita Vassena</b> , <i>Spain</i> <b>Georg Griesinger</b> , <i>Germany</i> <b>Ben Mol</b> , <i>Australia</i> <b>Joop Laven</b> , <i>Netherlands</i>	
Lab procedures	<ul style="list-style-type: none"> <li>• The automated IVF lab of the future</li> <li>• Perfect timings in the embryology lab: When to denude, when to fertilize, when to culture?</li> <li>• What is the optimal culture media?</li> <li>• Noninvasive embryo selection</li> </ul>	
Clinical procedures	<ul style="list-style-type: none"> <li>• Any value to reproductive immunology tests and treatments?</li> <li>• PCOS: Is menopause and fertility window delayed?</li> <li>• DuoStim or two stimulations - any proven advantage?</li> <li>• Recurrent implantation failure does not exist!</li> <li>• IUI deserves a place in the treatment of unexplained infertility</li> <li>• What are the clinical risks of freeze all?</li> </ul>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions



12:30-14:00	WORKSHOP ON UNDERSTANDING CURRENT ADD-ONS	HALL I
Capsule	Up to 74% of UK patients attending IVF received some sort of add-ons - none of which received the HFEA green "go ahead" light. Add-ons are expensive, sophisticated, time consuming and widely used, with the false pretext of providing better results. A summary of the situation was given 25 years ago: "much poor research arises because researchers feel compelled for career reasons to carry out research that they are ill equipped to perform and nobody stops them" (Altman DG, BMJ, 1994).	
Chairperson	<b>Zion Ben Rafael, Israel</b>	
12:30-12:50	End of endometrial scratching? <b>Ben Mol, Australia</b>	
12:50-13:10	ERA test - What are the reservations? <b>Zion Ben Rafael, Israel</b>	
13:10-13:30	Non-invasive PGD-A is the future! <b>Samir Hamamah, France</b>	
13:30-14:00	<u>Debate: End of freeze all?</u> Yes - Freeze all should be used carefully and by indication: <b>Abha Maheshwari, UK</b> No - Freeze all serves to circumvent faulty endometrium: <b>Bruce S. Shapiro, USA</b> Discussion	

**14:00-14:05 Break**

14:05-15:05	INDUSTRY SUPPORTED SESSION See page 103	HALL I
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**15:05-15:10 Break**

15:10-16:40	PGT-A: HELPFUL OR HARMFUL?	HALL I
Capsule	HFEA recently downgraded PGT-A from "Amber" to "Red", suggesting it has no proof. Are we all in agreement?	
Chairpersons	<b>Simon Fishel, UK</b> <b>Luca Gianaroli, Italy</b>	
15:10-15:40	<u>Debate: What happens after the STAR and ESTEEM studies trials that have failed to show better results? Should we stop proposing PGT-A to patients? Should we change our clinical attitude towards the test?</u> No: <b>Willem Verpoest, Belgium</b> Yes: <b>Sebastiaan Mastenbroek, Netherlands</b> Discussion	
15:40-16:10	<u>Debate: There are now studies indicating that up to 50% of 1PN embryos are normal. Should we discard them?</u> Yes: <b>Filippo Zambelli, Spain</b> No: <b>Rita Vassena, Spain</b> Discussion	
16:10-16:40	<u>Special countercurrent lecture: Technology versus biology, how biology presents a limitation to PGT-A</u> <b>Rajiv McCoy, USA</b>	

**16:40-17:00 Virtual exhibition and e-poster viewing**

17:00-18:30	PCOS	HALL I
Chairperson	<b>Bart Fauser</b> , <i>Netherlands</i>	
17:00-17:25	New aspects of the polycystic ovary syndrome <b>Joop Laven</b> , <i>Netherlands</i>	
17:25-17:45	AMH and its role in the pathophysiology of PCOS <b>Antonio La Marca</b> , <i>Italy</i>	
17:45-18:10	Implications of cardiometabolic dysfunction in PCOS women <b>Bart Fauser</b> , <i>Netherlands</i>	
18:10-18:30	Effects of a three-component lifestyle program on weight loss in women with PCOS <b>Geranne Jiskoot</b> , <i>Netherlands</i>	



## FRIDAY, NOVEMBER 20, 2020

### GYNECOLOGY – HALL II

09:00-10:30	CONTRACEPTION: THE UNDER-APPRECIATED BENEFITS	HALL II
Chairpersons	<b>Christian Egarter</b> , <i>Austria</i> <b>Johannes Bitzer</b> , <i>Switzerland</i>	
09:00-09:25	Irritable bowel syndrome <b>Vincenzo Stanghellini</b> , <i>Italy</i>	
09:25-09:50	Asthma and rheumatoid arthritis <b>Alessandra Graziottin</b> , <i>Italy</i>	
09:50-10:15	Optimizing psychosexual health with perimenopausal contraception <b>Johannes Bitzer</b> , <i>Switzerland</i>	
10:15-10:30	Discussion	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	ADVANCES IN HORMONAL AND NON-HORMONAL RESEARCH	HALL II
Chairperson	<b>Mark Brincat</b> , <i>Malta</i>	
11:00-11:40	<b>Debate: Should androgens be routinely offered to optimize quality of life in menopause?</b>	
11:00	For: <b>Alessandra Graziottin</b> , <i>Italy</i>	
11:15	Against: <b>Johannes Bitzer</b> , <i>Switzerland</i>	
11:30	Discussion	
11:40-12:05	How to overcome hormone resistance? <b>Ludwig Kiesel</b> , <i>Germany</i>	
12:05-12:30	New SERMS/TSECS: Can they be an HRT substitute? <b>Santiago Palacios</b> , <i>Spain</i>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions

12:30-14:00	NON-ABLATIVE AND MICRO-ABLATIVE LASERS IN GYNECOLOGY	HALL II
Capsule	LASER in medicine stands for a number of diverse devices. They radiate different energy at different wavelengths and produce different effects in different tissues. Er:YAG and CO2 lasers have been introduced, through last decade, for gynecology applications. Growing evidence supports non-ablative, and micro-ablative laser technology as an effective intervention for stress urinary incontinence, vulvo-vaginal atrophy, lichen sclerosus atrophicus, vaginal relaxation, etc. Despite of warnings from leading international organizations against the use of energy-based devices (EBDs) in certain fields of gynecology, contemporary evidence, that is going to be presented in this symposium, confirm safety and efficacy of laser treatment for genitourinary syndrome of menopause (GSM).	
Chairperson	<b>Ivan Fistonić</b> , <i>Croatia</i>	
12:30-12:50	Laser based vaginal treatments: Physical principles and biological effect <b>Menachem Alcalay</b> , <i>Israel</i>	
12:50-13:10	CO2 laser applications in gynecology <b>Stefano Salvatore</b> , <i>Italy</i>	
13:10-13:30	Potential of laser therapy in vulvar pathologies <b>Mark Brincat</b> , <i>Malta</i>	
13:30-13:50	Er: YAG vaginal laser therapy - hype or established treatment? <b>Ivan Fistonić</b> , <i>Croatia</i>	
13:50-14:00	Discussion	

#### 14:00-14:05 Break

<b>14:05-15:05</b>	<b>INDUSTRY SUPPORTED SESSION</b> See page 102	<b>HALL II</b>
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**15:05-15:10 Break**

<b>15:10-16:40</b>	<b>VULVAR PAIN AND CO-MORBIDITIES</b>	<b>HALL II</b>
Chairperson	<b>Ludwig Kiesel, Germany</b>	
15:10-15:35	Vulvar pains and co-morbidities: Data from 1183 cases <b>Alessandra Graziottin, Italy</b>	
15:35-16:00	Vagina as an androgen target <b>Linda Vignozzi, Italy</b>	
16:00-16:40	<u>Debate:</u> <b>Is laser treatment first line choice for Genitourinary Syndrome of Menopause (GSM)?</b>	
16:00	Yes: <b>Zdenko Vizintin, Slovenia</b>	
16:15	No: <b>Tim Hillard, UK</b>	
16:30	Discussion	

**16:40-17:00 Virtual exhibition and e-poster viewing**

<b>17:00-18:30</b>	<b>HPV</b>	<b>HALL II</b>
Chairperson	<b>Xavier Bosch, Spain</b>	
17:00-17:20	Natural history of HPV among females: Implications for control <b>Anna Barbara Moscicki, USA</b>	
17:20-17:40	Lessons learned from CC screening in KP: Intervals, primary HPV testing, how to limit the harms of screening, management by individual risk and impact of HPV vaccines <b>Walter Kinney, USA</b>	
17:40-18:00	What is new in preventive and therapeutic vaccines <b>John T. Schiller, USA</b>	
18:00-18:20	Real world effectiveness and duration of protection of HPV vaccination <b>Suzanne Garland, Australia</b>	
18:20-18:30	Q&A	

## SATURDAY, NOVEMBER 21, 2020

### GYNECOLOGY – HALL II

09:00-10:30	OVARIAN CANCER – NEW INSIGHTS AND CURRENT TREATMENT STANDARDS	HALL II
Chairpersons	<b>Jalid Sehouli</b> , <i>Germany</i> <b>Elena Braicu</b> , <i>Germany</i>	
09:00-09:20	Molecular understanding of ovarian cancer <b>Elena Braicu</b> , <i>Germany</i>	
09:20-09:45	Current role of primary surgery <b>Robert Armbrust</b> , <i>Germany</i>	
09:45-10:05	Maintenance therapy in advanced ovarian cancer <b>Klaus Pietzner</b> , <i>Germany</i>	
10:05-10:30	Relapsed ovarian cancer <b>Jalid Sehouli</b> , <i>Germany</i>	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	RECENT ADVANCES ON POI AND LINK WITH DNA REPAIR/CANCER GENES	HALL II
Chairperson	<b>Lisa Webber</b> , <i>UK</i>	
11:00-11:25	BRCA2 and Fancm mutants in primary ovarian insufficiency without cancer or Fanconi anemia trait <b>Micheline Misrahi</b> , <i>France</i>	
11:25-11:55	Understanding the genetics of POI is important in clinical practice for the management of affected women and their families <b>Micheline Misrahi</b> , <i>France</i>	
11:55-12:15	Is there a need for a POI network/database? <b>Nick Panay</b> , <i>UK</i>	
12:15-12:30	POI and National Genomics: The experience in England <b>Brianna Cloke</b> , <i>UK</i>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions

12:30-14:00	PCOS AT MENOPAUSE	HALL II
Chairperson	<b>Santiago Palacios</b> , <i>Spain</i>	
12:30-13:00	Is there an increased CVD risk in PCOS women? <b>Bart Fauser</b> , <i>Netherlands</i>	
13:00-13:30	Delayed fertility and later menopause in PCOS <b>Joop Laven</b> , <i>Netherlands</i>	
13:30-14:00	Should ovarian tissue reimplantation be considered for all women to postpone menopause? <b>Mark Brincat</b> , <i>Malta</i>	

#### 14:00-14:05 Break

14:05-15:05	ISMAAR SESSION: MILD IVF	HALL II
Chairperson	<b>Rene Frydman, France</b>	
14:05-14:45	<b>Debate: Should mild IVF be the new norm in the post-COVID era?</b>	
14:05	For: <b>Geeta Nargund, UK</b>	
14:20	Against: <b>Georg Griesinger, Germany</b>	
14:35	Discussion	
14:45-15:05	Ovarian placental shift <b>Georg Griesinger, Germany</b>	

#### 15:05-15:10 Break

15:10-16:40	ENDOMETRIOSIS	HALL II
Chairpersons	<b>Jessica Ybanez-Morano, USA</b> <b>Olivier Donnez, Belgium</b>	
15:10-15:35	Long term risk of cancer in women carrying unoperated ovarian endometriomas: Immediate surgery, delayed surgery or never surgery? <b>Paolo Vercellini, Italy</b>	
15:35-15:55	State-of-the-art of medical therapy or how to explain pain in endometriosis <b>Sylvia Mechsner, Germany</b>	
15:55-16:20	<u>Special countercurrent lecture:</u> The role of miRNA as a marker for endometriosis <b>Ludwig Kiesel, Germany</b>	
16:20-16:40	Vaginal microbiome: A new frontier into antibiotic resistant superbugs <b>Gary Ventolini, USA</b>	

#### 16:40-17:00 Virtual exhibition and e-poster viewing

17:00-18:30	SLS: THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS	HALL II
Chairperson	<b>Jessica Ybanez-Morano, USA</b>	
17:00-17:20	The future in fertility surgery <b>Mona Orady, USA</b>	
17:20-17:40	Dealing with parametrium endometriosis <b>Thiers Soares Raymundo, Brazil</b>	
17:40-18:05	Updates on reduced site laparoscopy <b>Jessica Ybanez-Morano, USA</b>	
18:05-18:30	Stop resecting septum <b>Fulco van der Veen, Netherlands</b>	



## FRIDAY, NOVEMBER 20, 2020

### FETOMATERNAL MEDICINE – HALL III

09:00-10:30	PRENATAL DIAGNOSIS	HALL III
Capsule	NIPT - what is the experience after millions of cases and how to counsel about it properly?	
Chairpersons	<b>Wolfgang Henrich</b> , <i>Germany</i> <b>Boris Tutschek</b> , <i>Switzerland</i>	
09:00-09:30 09:00 09:10 09:20	<u>Debate: NIPT- a screening or diagnostic method for all</u> Diagnostic by indication: <b>Wolfgang Holzgreve</b> , <i>Germany</i> Screening - for all including all ART: <b>Gerard Visser</b> , <i>Netherlands</i> Discussion	
09:30-10:00	Developments in cell-based non-invasive prenatal screening <b>Michael J. Sinosich</b> , <i>Australia</i>	
10:00-10:30	Should we offer NIPT to diseases (ex CF, SMA) that progress towards gene therapy? <b>Wolfgang Holzgreve</b> , <i>Germany</i>	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	PERIPARTUM COMPLICATIONS	HALL III
Chairpersons	<b>Diogo Ayres de Campos</b> , <i>Portugal</i> <b>Larry Hinkson</b> , <i>Germany</i>	
11:00-11:25	Periconceptional appropriate nutrition <b>Gian Carlo Di Renzo</b> , <i>Italy</i>	
11:25-11:45	Tricks and tips to preserve the uterus with advanced procedures (AIP) <b>Thorsten Braun</b> , <i>Germany</i>	
11:45-12:05	Cardiac disease in pregnancy and postpartum <b>Petra Gehle</b> , <i>Germany</i>	
12:05-12:30	Acute abdomen during pregnancy <b>Wolfgang Henrich</b> , <i>Germany</i>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions

12:30-14:00	FERTILITY PRESERVATION (Part of the Infertility/ART/IVF track)	HALL III
Chairpersons	<b>Laura Rienzi</b> , <i>Italy</i> <b>Marie-Madeleine Dolmans</b> , <i>Belgium</i>	
12:30-12:50	Fertility preservation for cancer women <b>Marie-Madeleine Dolmans</b> , <i>Belgium</i>	
12:50-13:25 12:50 13:00 13:10	<u>Debate: Fertility preservation (social freezing) for all women?</u> Yes: <b>Rita Vassena</b> , <i>Spain</i> No: <b>Zion Ben Rafael</b> , <i>Israel</i> Discussion	
13:25-14:00 13:25 13:35 13:45	<u>Debate: Fertility preservation for women with endometriosis?</u> Yes: <b>Jacques Donnez</b> , <i>Belgium</i> No: <b>Edgardo Somigliana</b> , <i>Italy</i> Discussion	

#### 14:00-14:05 Break

14:05-15:05	GLOBAL AND WOMEN'S HEALTH	HALL III
Chairpersons	<b>Andreas Ulrich</b> , <i>Germany</i> <b>Murat Gültekin</b> , <i>Turkey</i>	
14:05-14:25	Screening of HPV: Options and limits <b>Andreas Kaufman</b> , <i>Germany</i>	
14:25-14:45	Impact of COVID-19 on clinical management of women with gynecological cancer <b>Sara Nasser</b> , <i>Germany</i>	
14:45-15:05	Challenges of communication in the pandemic era <b>Jalid Sehouli</b> , <i>Germany</i>	

#### 15:05-15:10 Break

15:10-16:40	GESTATIONAL DIABETES MELLITUS (GDM)	HALL III
Chairpersons	<b>Dan Farine</b> , <i>Canada</i> <b>Ute Schäfer-Graf</b> , <i>Germany</i>	
15:10-15:40 15:10 15:20 15:30	<u>Debate:</u> <b>Should oral hypoglycemic drugs be used in Gestational Diabetes Mellitus (GDM)?</b> Yes: <b>Yariv Yogev</b> , <i>Israel</i> No: <b>Gerard Visser</b> , <i>Netherlands</i> Discussion	
15:40-16:10 15:40 15:50 16:00	<u>Debate:</u> <b>Induction of labor for women with diabetes in pregnancy?</b> Yes: <b>Yariv Yogev</b> , <i>Israel</i> No: <b>Ute Schäfer-Graf</b> , <i>Germany</i> Discussion	
16:10-16:40 16:10 16:20 16:30	<u>Debate:</u> <b>Should obese women be advised to lose weight in pregnancy?</b> Yes: <b>Thorsten Braun</b> , <i>Germany</i> No: <b>Yariv Yogev</b> , <i>Israel</i> Discussion	

#### 16:40-17:00 Virtual exhibition and e-poster viewing

17:00-18:15	HIGH RISK PREGNANCY	HALL III
Chairperson	<b>Gerard Visser</b> , <i>Netherlands</i>	
17:00-17:25	Use of proteomics for detections of Rare Autosomal Trisomies (RATs) and aneuploidies beyond reach of cfDNA <b>Michael J. Sinosich</b> , <i>Australia</i>	
17:25-17:50	Treating gestational diabetes in twins: More harm than good? <b>Nir Melamed</b> , <i>Canada</i>	
17:50-18:15	Vertical SARS-COV2 transmission support fetal/newborn resistance to infection <b>Eytan Barnea</b> , <i>USA</i>	

## SATURDAY, NOVEMBER 21, 2020

### FETOMATERNAL MEDICINE – HALL III

09:00-10:30	GENERAL HEALTH AND FERTILITY	HALL III
Chairperson	<b>Jens Peter Bonde</b> , <i>Denmark</i>	
09:00-09:20	Prenatal and postnatal exposure to endocrine disrupting chemicals and male reproductive disorders <b>Jens Peter Bonde</b> , <i>Denmark</i>	
09:20-09:45	Bisphenol A and reproductive toxicology <b>Gilbert Schönfelder</b> , <i>Germany</i>	
09:45-10:05	Impact of parental over- and underweight on the health of offspring <b>Juan Garcia Velasco</b> , <i>Spain</i>	
10:05-10:30	From micromanipulation to nanomanipulation in ART <b>Gerald Schatten</b> , <i>USA</i>	

#### 10:30-11:00 Virtual exhibition and e-poster viewing

11:00-12:30	ROUND TABLE DISCUSSION ON PRETERM LABOUR	HALL III
Chairpersons	<b>Wolfgang Henrich</b> , <i>Germany</i> <b>Yariv Yogev</b> , <i>Israel</i>	
Discussants	<b>Diogo Ayres de Campos</b> , <i>Portugal</i> <b>Asma Khalil</b> , <i>UK</i> <b>Thorsten Braun</b> , <i>Germany</i> <b>Gerard Visser</b> , <i>Netherlands</i> <b>Birgit Arabin</b> , <i>Germany</i>	
	<ol style="list-style-type: none"> <li>1. Cervical length screening by indication or for all? When</li> <li>2. Progesterone, pessary or cerclage?</li> <li>3. Should progesterone be used after arrested PTL?</li> <li>4. Pessary for PTL, in singleton and multiple pregnancy</li> <li>5. Is there a role for maintenance tocolysis?</li> <li>6. Emergency cerclage, when? Which technique?</li> <li>7. Should women with arrested PTL or PTL in the previous labor be treated? With what?</li> <li>8. Need for steroids at 34-37 debate</li> <li>9. What is the appropriate management after previous pregnancy with placental complications?</li> <li>10. When to deliver small babies near term?</li> </ol>	

#### 12:30-15:05 Virtual exhibition, e-poster viewing and early afternoon sessions

12:30-14:00	CAESAREAN SECTION AND DELIVERY	HALL III
Chairpersons	<b>Wolfgang Henrich</b> , <i>Germany</i> <b>Gian Carlo Di Renzo</b> , <i>Italy</i>	
12:30-13:00 12:30 12:40 12:50	<u>Debate: Induction of labor after previous caesarean section</u> Yes: <b>Yariv Yogev</b> , <i>Israel</i> No: <b>Ariel Many</b> , <i>Israel</i> Discussion	
13:00-13:15	When to treat and when not uterine niche <b>Olivier Donnez</b> , <i>Belgium</i>	
13:15-13:45 13:15 13:25 13:35	<u>Debate: Women after 3rd or 4th degree perineal tear should be delivered by caesarean section</u> Yes: <b>Ariel Many</b> , <i>Israel</i> No: <b>Yariv Yogev</b> , <i>Israel</i> Discussion	
13:45-14:00	Induction of labour does not increase the caesarean section rate <b>Ben Mol</b> , <i>Australia</i>	

**14:00-14:05 Break**

14:05-15:05	ULTRASOUND IN PREGNANCY	HALL III
Chairpersons	<b>Boris Tutschek</b> , <i>Switzerland</i> <b>Wolfgang Henrich</b> , <i>Germany</i>	
14:05-14:20	1 <sup>st</sup> trimester ultrasound screening <b>Rabih Chaoui</b> , <i>Germany</i>	
14:20-14:35	2 <sup>nd</sup> trimester ultrasound screening <b>Stuart Campbell</b> , <i>UK</i>	
14:35-14:50	Ultrasound in the delivery room <b>Tullio Ghi</b> , <i>Italy</i>	
14:50-15:05	Ultrasound in the postpartum period <b>Wolfgang Henrich</b> , <i>Germany</i>	

**15:05-15:10 Break**



15:10-16:40	PRE-ECLAMPSIA TOXEMIA (PET) AND INTRAUTERINE GROWTH RETARDATION (IUGR)	HALL III
Capsule	Can we predict and prevent pre-eclampsia toxemia (PET)?	
Chairpersons	<b>Stefan Verlohren</b> , <i>Germany</i> <b>Luigi Raio</b> , <i>Switzerland</i>	
15:10-15:30	Value of pre-eclampsia screening in the first trimester <b>Stefan Verlohren</b> , <i>Germany</i>	
15:30-15:50	What is the appropriate growth curve to be used for fetal assessment? <b>Nir Melamed</b> , <i>Canada</i>	
15:50-16:10	The impact of sFlt/PlGF ratio on the prediction and management of preeclampsia <b>Luisa Pinto</b> , <i>Portugal</i>	
16:10-16:40	<u>Special Countercurrent lecture</u> : Managing pregnancies at the limits of viability <b>Dan Farine</b> , <i>Canada</i>	

#### 16:40-17:00 Virtual exhibition and e-poster viewing

17:00-18:30	INTRAPARTUM MONITORING	HALL III
Chairperson	<b>Diogo Ayres de Campos</b> , <i>Portugal</i>	
17:00-17:25	ST analysis: A false hope? <b>Diogo Ayres de Campos</b> , <i>Portugal</i>	
17:25-17:45	Fetal arrhythmias <b>Christoph Berg</b> , <i>Germany</i>	
17:45-18:10	Antepartum ultrasound in labor ward <b>Boris Tutschek</b> , <i>Switzerland</i>	
18:10-18:30	US external version in breech presentation <b>Larry Hinkson</b> , <i>Germany</i>	

## *E-Poster Presentations*

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### **ART/IVF**

PREDICTORS OF LIVE BIRTH FOLLOWING A SINGLE EMBRYO TRANSFER IN FRESH AND FROZEN IVF/ICSI CYCLES

**Devini Ameratunga**, *Australia*

EMBRYO QUALITY AND CHROMOSOMAL STATUS. IS THERE RELATIONSHIP BETWEEN BOTH?

**Marta Ariza**, *Spain*

AUTOLOGOUS INSEMINATIONS ARE LESS EFFECTIVE THAN USING DONORS

**Marta Armas Roca**, *Spain*

ACUPUNCTURE AND FEMALE INFERTILITY: A LITERATURE REVIEW OVER STUDIES PUBLISHED IN THE LAST 5 YEARS

**Tatiana Branco Vaz**, *Portugal*

NOVEL METHODOLOGY OF SPERM SELECTION: A LOGIC CENTRIFUGATION-FREE ALTERNATIVE TO MICROFLUIDICS

**Yolanda Cabello**, *Spain*

MULTIVARIATE MODELS FOR ASSESSING SUCCESS IN IN VITRO FERTILIZATION. SYSTEMATIC REVIEW AND META-ANALYSIS OF PREDICTIVE FACTORS INFLUENCING RESULTS

**Maria Carrera**, *Spain*

DIAGNOSTIC ACCURACY OF SUBMUCOSAL FIBROIDS IN INFERTILE WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS

**Maria Carrera**, *Spain*

CONSTRUCTION AND VALIDATION OF A MULTIVARIATE PREDICTIVE MODEL OF TWIN PREGNANCIES AFTER DAY 3 FRESH DOUBLE EMBRYO TRANSFERS

**Maria Carrera**, *Spain*

POSITIVE ASSOCIATION OF POLYMORPHISM IN CYP19A1 GENE WITH FEMALE INFERTILITY SUSCEPTIBILITY

**Maria Manuel Casteleiro Alves**, *Portugal*

IN VITRO FECUNDATION AS SECOND OPTION FOR COUPLES DIAGNOSED WITH UNEXPLAINED INFERTILITY

**Caterina Ceccarelli**, *Spain*

PERINATAL RESULTS IN IN VITRO FECUNDATION CYCLES FOR UNEXPLAINED INFERTILITY

**Caterina Ceccarelli**, *Spain*

MISCARRIAGE RATE AFTER ASSISTED REPRODUCTIVE TECHNOLOGIES

**Ines Lourenco**, *Portugal*

PREIMPLANTATION EMBRYONIC MOSAICISM AND MATERNAL AGE IN INVITRO FERTILIZATION CYCLES

**Maria Jose Mendiola**, *Peru*

ARTIFICIAL INSEMINATION AS FIRST CHOICE IN COUPLES WITH UNEXPLAINED INFERTILITY

**Carla Mendoza**, *Spain*

PREDICTORS OF SUCCESS FOR ARTIFICIAL INSEMINATIONS IN COUPLES WITH UNEXPLAINED STERILITY

**Carla Mendoza**, *Spain*

LIVE BIRTH RATES AFTER ASSISTED REPRODUCTIVE TECHNIQUES OF ADVANCED AGED WOMEN

**Gulnaz Sahin**, *Turkey*

OIL EQUILIBRATION TIME HAS AN IMPORTANT IMPACT ON BLASTOCYST DEVELOPMENT

**Marta Sanchez De Burgos**, *Spain*



IS MORE BETTER? PREDICTING THE LIKEHOOD OF LIVE BIRTH ACCORDING TO THE NUMBER OF OOCYTES RETRIEVED AFTER OVARIAN STIMULATION FOR IN VITRO FERTILIZATION

**Marina Sousa Gomes**, *Portugal*

PRESERVATION OF PRIMORDIAL FOLLICLE RESERVE BY PHARMACOLOGICAL INHIBITORS TARGETING THE PI3K/PTEN/AKT, MTOR AND JNK PATHWAYS IN MURINE OVARIAN CULTURE

**Carmen Terren**, *Belgium*

IMPROVING MATERNAL HEALTH: DO SINGLETON PREGNANCIES EFFECTIVELY MITIGATE THE MEDICAL, ETHICAL AND LEGAL RISKS ASSOCIATED WITH INVASIVE FERTILITY TREATMENT?

**Anna Ulyanenkova**, *USA*

DOES BODY MASS INDEX EFFECT IN VITRO FERTILISATION OUTCOME IN POLYCYSTIC OVARIAN SYNDROME?

**Arzu Yurci**, *Turkey*

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## DIAGNOSTIC PROCEDURES

A RELIABLE METHOD TO ASSESS CERVICAL STIFFNESS, TOWARDS THE PREDICTION OF PRETERM BIRTH

**Sabrina Badir**, *Switzerland*

AUDIT ON ADHERENCE OF DIAGNOSTIC MODALITIES AND MANAGEMENT PROTOCOL OF PATIENTS PRESENTING WITH SUSPECTED PRETERM LABOUR AT DAY ASSESSMENT UNIT OF A DISTRICT GENERAL HOSPITAL IN UK

**Indranil Banerjee**, *UK*

HERLYN-WERNER-WUNDERLICH SYNDROME – FEATURES OF DIAGNOSIS AND TREATMENT

**Nataliya Veresnyuk**, *Ukraine*

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## FETOMATERNAL MEDICINE

VUS IN HRG GENE: A CAUSE FOR RECURRENT MISCARRIAGE, PRETERM LABOUR, IVF FAILURE

**Kriti Agarwal**, *India*

RUPTURED RUDIMENTARY HORN PREGNANCY MASQUERADING AS CESAREAN SCAR RUPTURE IN THIRD TRIMESTER

**Kriti Agarwal**, *India*

PREECLAMPSIA: POTENTIAL BIOMARKERS FOR DIAGNOSIS AND TARGETS FOR THERAPY

**Ana Rita Alves**, *Portugal*

CONTROLLED BALLON TAMPONADE FOR THE MANAGMENT OF MASSIVE POSTPARTUM HAEMORRHAGE

**Natalia Artymuk**, *Russia*

COVID-19 AND PREGNANCY IN SIBERIA AND FAR EAST

**Natalia Artymuk**, *Russia*

AN AUDIT OF CAESAREAN SECTION FOR ARREST OF ACTIVE PHASE LABOUR AND THE USE OF OXYTOCIN AT TWEED HOSPITAL

**Jessica Benton**, *Australia*

PLACENTAL ANATOPATHOLOGICAL STUDY IN CASES OF THREAT PRE-TERM DELIVERY

**Sara Bernardes Da Cunha**, *Portugal*

UPTAKE AND OUTCOMES OF VAGINAL BIRTH AFTER CAESAREAN (VBAC) IN NHS LANARKSHIRE

**Edie Booth**, *UK*

ACTIVE TERMINATION OF TERM PREGNANCIES IN FETAL GROWTH RESTRICTION - QUESTIONING CURRENT PRACTICES

**Joao Coimbra**, *Portugal*

PREGNANCY LOSS, RANDOM EVENTS AND COSMIC RAYS

**Piet De Groen**, *USA*

DO VEGETARIAN PREGNANT WOMEN NEED FOOD SUPPLEMENTS?

**Natalia Del Valle Sanchez Baudo**, *Spain*

A SUCCESSFUL PREVENTION OF PRE-ECLAMPSIA WITH ASPIRIN, VITAMIN D AND CALCIUM SUPPLEMENTATION – A CASE REPORT

**Emina Ejubovic**, *Bosnia and Herzegovina*

APLASIA CUTIS CONGENITA ON LUMBOSACRAL AREA - A CHALLENGING DIFFERENTIAL DIAGNOSIS

**Patricia Ferreira**, *Portugal*

ADVANCED MATERNAL AGE AND LOW BIRTH WEIGHT

**Patricia Ferreira**, *Portugal*

CERVICAL ADENOCARCINOMA IN SITU DIAGNOSED IN A LATE SECOND TRIMESTER PREGNANCY: A CASE REPORT

**Mariana Lira Morais**, *Portugal*

PERIVIALE BIRTH: CAUSES AND RECURRENCE RISK

**Ana Rita Mateus**, *Portugal*

PERIVIALE BIRTH - MODE OF DELIVERY

**Ana Rita Mateus**, *Portugal*

FETAL GROWTH RESTRICTION (FGR): MORE THAN LOW BIRTHWEIGHT; MEASURES OF ASYMMETRIC FGR BETTER DEFINE THE GROUP 'AT RISK' GROUP THAN LOW BIRTHWEIGHT FOR GESTATIONAL AGE (SGA)

**Roger McMaster-Fay**, *Australia*

THE REBOA TECHNIQUE TO REDUCE MORBIDITY IN PATIENTS WITH KNOWN PLACENTA ACCRETA SPECTRUM DISORDERS: A CASE SERIES

**Sharron Moeraert**, *Belgium*

DELIVERY ROUTE IN PREGNANT WOMEN WITH PREVIOUS CESAREAN SECTION IN OUR HOSPITAL

**Silvia Morales Munoz**, *Spain*

PRENATAL DIAGNOSIS OF SPLIT SPINAL CORD MALFORMATION TYPE 1 – TWO DIFFERENT CASES, ONE SAME OUTCOME

**Sara Nunes**, *Portugal*

PERIPARTUM CARDIOMYOPATHY, A RARE CAUSE OF POSTPARTUM DYSPNEA

**Sara Nunes**, *Portugal*

SEQUENTIAL INSTRUMENTATION IN OPERATIVE VAGINAL DELIVERIES – ARE THE RISKS OF MATERNAL AND NEONATAL MORBIDITY TOO HIGH?

**Elizabeth O'Donnell**, *UK*

FETAL VENTRICULOMEGALY: SHOULD SAME INVESTIGATION BE OFFERED IN ALL CASES?

**Rodrigo Pereira Mata**, *Portugal*



MCDA PREGNANCY – NEC AS A CONSEQUENCE OF TTTS

**Ines Reis**, *Portugal*

CORRECTION OF THE IRON CONTENT IN THE BODY OF WOMEN AT THE STAGE OF PREPARATION FOR PREGNANCY

**Iryna Rudenko**, *Ukraine*

AUTOIMMUNE HEMOLYTIC ANEMIA IN PREGNANCY AND A RARE COMPLICATION OF ITS MANAGEMENT: A CASE REPORT

**Raphael Santos**, *Philippines*

PLACENTAL INDEX, PLACENTAL CHARACTERISTICS, BIRTHWEIGHT, AND NEONATAL OUTCOME IN PREGNANCIES

**Leo Simanjuntak**, *Indonesia*

ANXIETY LEVELS AND RELATED FACTORS IN TERM PREGNANT WOMEN UNDERGOING CAESAREAN SECTION

**Patrick Anando Simanjuntak**, *Indonesia*

PERIPARTUM CARDIOMYOPATHY: A CASE REPORT

**Catarina Soares**, *Portugal*

ANALYSIS OF LEPTIN CONCENTRATION IN THE BLOOD SERUM OF WOMEN GIVING BIRTH AND IN THE UMBILICAL BLOOD FROM PROPERLY DEVELOPING PREGNANCIES AND PREGNANCIES WITH SELECTED COMPLICATIONS

**Malgorzata Stefaniak**, *Poland*

TELEMETRIC INTERVENTIONS IN THE MANAGEMENT OF WOMEN WITH GESTATIONAL DIABETES MELLITUS

**Stefanie Stichling**, *Germany*

NOVEL INSIGHTS IN GESTATIONAL DIABETES MELLITUS CARE BY APPROACHING MOBILE HEALTH APPLICATIONS (MHEALTH-APPS)

**Stefanie Stichling**, *Germany*

POOR SLEEP IS ASSOCIATED WITH HIGHER BLOOD PRESSURE IN PREGNANCY AND HIGHER UTERINE ARTERY PULSATILITY INDEX

**Yafang Tang**, *Singapore*

INCIDENCE OF MYCOPLASMA HOMINIS, UREAPLASMA UREALYTICUM AND PREGNANCY OUTCOME

**Ilir Tasha**, *Albania*

NIPT VERSUS AMNIOCENTESIS IN FIRST TRIMESTER SCREENING FOR CHROMOSOMAL ABNORMALITIES IN PATIENTS WITH HIGH RISK OF TRISOMY 21,18 AND INTERMEDIATE-RISK OF TRISOMY 21

**Ilir Tasha**, *Albania*

FETOPLACENTAL MOSAICISM AND NON-INVASIVE PROCEDURE TESTING (CASE STUDY)

**Ilir Tasha**, *Albania*

UREAPLASMA UREALYTICUM AND MYCOPLASMA HOMINIS AMONG PREGNANT WOMEN

**Ilir Tasha**, *Albania*

ASCENDANT INTRAUTERINE INFECTION OF CANDIDA ALBICANS IN THE PREGNANTS WITH SYPHILIS

**Tetiana Yaremchuk**, *Ukraine*

BACTERIOPHAGES IN PREVENTION OF RECURRENT VAGINAL INFECTIONS FOR PREGNANT WOMEN

**Tatiana Zefirova**, *Russia*

EFFECT OF INTRAVENOUS IRON ON PERINATAL OUTCOMES IN PREGNANT WOMEN WITH ANEMIA

**Tatiana Zefirova**, *Russia*

## GYNECOLOGICAL ONCOLOGY

CERVICAL CANCER HPV NEGATIVE

**Sara Bernardes Da Cunha**, *Portugal*

GRANULOSA CELL TUMORS – TWO DISTINCT CLINICAL COURSES

**Carolina Carneiro**, *Portugal*

INTRAOPERATIVE USE OF INDOCYANINE GREEN TO DELINEATE PLACANTAL INVASION DURING ROBOTIC PERIPARTUM HYSTERECTOMY FOR MORBIDLY ADHERENT PLACENTA

**Katherine L. Dengler**, *USA*

OVARIAN CANCER: LIFESTYLE, DIET AND NUTRITION

NUTRITION AND CANCER, DOI:10.1080/01635581.2020.1792948

**Sherif Elsherif**, *UK*

OVERCOMING CHALLENGES OF MINIMALLY INVASIVE EXTRAFASCIAL HYSTERECTOMY IN THE POST RADICAL TRACHELECTOMY PATIENT

**Payam Katebi Kashi**, *USA*

VULVAR CANCER AND SURGERY: PROGNOSTIC FACTORS AND OUTCOMES

**Ionescu Sinziana**, *Romania*

THREE CANCERS (CERVIX, OVARY, RECTAL), ONE PATIENT: WHICH WILL RELAPSE? HOW MANY SURGERIES ARE TOO MANY?

**Ionescu Sinziana**, *Romania*

PERFORATION OF THE SIGMOID COLON – A RARE CLINICAL PRESENTATION OF THE OVARIAN TUMOR

**Ana Soares**, *Portugal*

POSTMENOPAUSAL INVASIVE MOLE WITH UTERINE RUPTURE

**Marina Sousa Gomes**, *Portugal*

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## GYNECOLOGY

ENDOMETRIAL RECEPTIVITY CHARACTERISTICS IN WOMEN WITH DIFFERENT FUNCTIONAL ACTIVITY OF OVARIAN CORPUS LUTEUM

**Natalia Aganezova**, *Russia*

RETAINED PRODUCTS OF CONCEPTION FOLLOWING SURGICAL MANAGEMENT OF CERVICAL ECTOPIC PREGNANCY

**Marrwah Ahmadzai**, *Australia*

A RARE CASE OF LABIAL CAVERNOUS LYMPHANGIOMA

**Marrwah Ahmadzai**, *Australia*

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# *Abstracts*

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## INVITED SPEAKER ABSTRACTS

### VERTICAL SARS-COV2 TRANSMISSION SUPPORT FETAL/NEWBORN RESISTANCE TO INFECTION

Eytan R. Barnea MD, FACOG

S.I.E.P., The Society for the Investigation of Early Pregnancy, NY, NY, USA

**Problem:** At first glance, maternal viral infection inevitably should cause fetal infection. However, each pathogen follows a different path, irrespective of maternal disease severity - some teratogenic, others exhibit minimal/no symptoms. Critical analysis is due to SARS-COV2 heterogeneity with respect to maternal/fetal vertical transmission infection.

**Methods:** Delineate SARS-COV2 as continuum vertical transmission from conception until post-delivery. Address that despite maternal vulnerability and associated placenta/membrane infection the fetus/newborn is rarely infected (mostly asymptomatic) reflecting innate fetal resilience against infection. **Results:** Other bacterial/viral infections diagnosis and management should clarify/frame current SARS COV2 clinical observations. Delineate caveats for minimal fetal infection: 1. Most infected patients are promptly delivered, treated with available various medications, antiviral/antibiotics including also steroids helping both in reducing mother/fetus inflammation and mature the fetus lung. 2. Respiratory infection severity varies, rarely transmitted through circulation reaching the placenta. Placental ACE2 protein expression at term is low but may still protect (placental surface is large / has active local immunity / may shield and/or facilitate fetal infection). Ensuing minimal fetal infection may reflect local resilience observed also in the newborn. 3. Newborn appears healthy however, for IgM antibody titer to develop- requires >4 days, to confirmed by IgG >2weeks later. PCR based viral test is carried out through nasal or rectal swab however, infection is mostly transplacental blood-born however, blood viral titers are rarely tested- due to assay sensitivity. 4. Peripartum/Intrapartum/postpartum infection patient/family/staff are not tested unless symptomatic-real infection rate remains unknown. 5. Reassuring that newborn can breast-fed (milk not infected) and longer-term outcome suggest lessened postnatal vulnerability. **Conclusion:** Minimizing infection, developing sensitive blood tests is imperative since long term SARS-COV2 sequelae remain a concern, i.e. adults (neurologic, cardiac). Lessons learnt from other rare beta-corona infections (SARS-COV and MERS) could be informative in upcoming mutating virus reality.

### ERA TEST: WHAT ARE THE RESERVATIONS?

Zion Ben Rafael MD, Mordechai Ben David MD.

Founder and Co-Chairperson, COGI Congress. Department of OB/GYN, Laniado Medical Center, Netanya, Israel. Affiliated with the Rappaport Faculty of Medicine, Technion, Haifa, Israel

This review addresses the limitations of the ERA methodology to increase implantation. From the assumed inconsistency of the endometrial biopsy, through the variable number of genes that were found to be dysregulated in an endometrium samples without the embryonal induced effect, the failure to account for the simultaneous serum progesterone level, the expected low percentage of patients who need this add-on procedure, to the difficulties in synchronizing the endometrium with hormone replacements in successive cycles and the inherent perinatal risks associated with across the board frozen-thawed embryos; Without a gold standard to compare, the claim that the window of implantation (WOI) might be off

by +12 hours only, requires a good argument for the advantage it provides to human procreation, knowing that embryos can linger for days before actual embedding start and that the window is of few days. Like all other add-ons, it is doubtful whether its use can significantly enhance implantation and success rate.

### REPEATED IMPLANTATION FAILURE (RIF): A MISLEADING NON-STANDARDIZED DEFINITION THAT AFFECTS THE QUALITY OF PUBLICATION

Zion Ben Rafael MD, Amir Weintraub, Mordechai Ben David MD

Founder and Co-Chairperson\*, COGI Congress. Department of OB/GYN and IVF Unit, Laniado Medical Center, Netanya, Israel. Affiliated with the Rappaport Faculty of Medicine, Technion, Haifa, Israel

Every IVF-failure is a stressful situation for patients and caregivers. Patients who are exposed to endless lay-press stories and publications fear that they have been misdiagnosed or mistreated, while physician who are in constant competition in this highly privatized sector fear that the failure will result in drop-outs. Patients have limited financial and psychological resources, after several failures the pressure to "do something" comes from patients and caregivers alike and they are chosen from a long list of possible invasive and non-invasive costly adjuvant solutions collectively named "add-ons", and a plethora of "home-made" stimulation protocols mixing various ideas, drugs and timings, that gives the impression of moving forwards, despite the lack of evidences to their efficacy. The term "Repeated Implantation Failure (RIF)" that was coined after 1-3 failures to denote that a change in the treatment should be done, but even 3 failures are not significant with the current failure rate of over 80%! RIF does not seem to be a real diagnosis that is based on a defined etiology, but rather a iatrogenic invention (Somigliana E. et al 2017, Evers JHL 2016). RIF does not imply a need for a change and so it is highly possible that the costly add-ons treatments are offered not to real failures but rather to a normal IVF population that need only to persevere and stay in the game, until success. Furthermore, RIF serves as an junction point of recruitment of patients for randomized control trials (RCT) with the pretext that their chances are impaired and addition of add-on can improve their chances of success. But, the true expectation after 1-3 failures in the control group should not be different than the clinic background, and that the study group should reach better than the mean results, which is not the case in most studies. Examples of studies where the differences between the study and the control groups, were due to low success in the control rather than higher results in study group, explains why many times initial RCT are rejected by later larger more accurate RCT's and meta-analysis.

### FERTILITY PRESERVATION (SOCIAL FREEZING) FOR ALL WOMEN: "NO"

Zion Ben Rafael MD\*, Mordechai Ben David MD

IVF Unit, and Department of Ob/Gyn, Laniado Medical Center, Israel, \*Founder and Co-Chairman of the Congress on Controversies in Obstetrics Gynecology and Infertility (COGI)

Delayed childbearing in affluent countries and the financial crisis of the Y-generation contribute to dramatic decline in birth rate. Social oocytes freezing (SOF) has fueled the

imagination of patients and doctors to offer it as a solution to single presumably fertile women to preserve their potential by egg banking at early age.. some are calling on governments to support large scale “fertility preservation”, but is it cost-effective? SOF is a sort of an expensive insurance, where future utilization is unknown. Theoretical studies have suggested that SOF is cost-effective only with about >50% usage rate, and when getting married is not set as a condition for usage. However, maximal possible utilization of the frozen eggs is much lower for each age group especially young one. Recent studies found usage rates of 3.1%-9.3% which sets the cost of each extra live birth at a stunning figure of >\$600,000-1,000,000. As IVF is being privatized and business-driven it's hard for experts to decipher scientific from business-oriented claims. Cost-effectiveness of SOF is far less than being stated to the private and the society. These facts put the responsibility on the shoulder of the treating physician who should inform the patients about the true chance to utilize the eggs, the age to freeze and possible alternative.

#### Review

Delayed marriage, late childbearing especially among the affluent countries and the financial crisis of the Y-generation contribute, in some countries, to the dramatic decline in birth rate and population. Nothing has changed in women's physiology that allows to deliberately postponed childbearing. pregnancies and deliveries should ideally be completed before a woman reaches age 35, at which point fertility tends to drop at a faster rate. Fertility drops annually: 1-4% before 35, 15% after 35, and 35% after 40 (Malchau et al 2017). At 35 about 35-40% of women will face difficulties in conceiving increasing after 40 years to over 60% of women. The reasons for this decrease in fertility are numerous. The first and most important reason is the “aging ovary”-a sharp drop in the number of oocytes in the ovary with increasing age. There is also an increase in incidence of the so-called “mechanical infertility”, pelvic adhesions or blocked tubes-because of previous pelvic infections, pelvic operations, cystectomy or endometriosis. Also, uterine fibroids and the operations to remove them can potentially damage the uterine, tubal or pelvic architecture. Male factor infertility, which can be responsible for or exists concomitantly with female infertility, affects almost half the cases and increases with age. As physicians, we cannot influence the trend of delayed marriage nor solve the financial problems of youth, which require governmental reform, we also cannot influence - beyond providing education - the changes in delayed childbearing which is related, among other factors, to a longer life expectancy. Women are usually aware of the risks of delayed childbearing, but they have a subjective sense of security amidst the popular publications that fertility treatments and IVF can help even in older age and recently that egg banking might be the ultimate solution, so they freeze and wait for the right partner or the right time, or until it's gets to be too late. Facts shows that women decide on egg banking at a mean age of >37 years, an age which is later than the medical community suggests. But do they ever use them anyhow? (Cobo et al. , 2016, Hammarberg et al., 2017). Does the “crowd wisdom” perceived something that we physicians with the eagerness to provide a perfect, even if costly solutions are missing? Maybe. Infertility treatments particularly IVF can help in achieving pregnancy in most of the cases depending on the age, but there are cases where IVF often fail. The most challenging indication for IVF is poor ovarian reserve and the age-related decrease in fertility, which is associated with a low

number of poor quality eggs, chromosomal abnormalities and higher incidence of miscarriages. The possible evolutionary explanation for these processes, which limits fertility several years before menopause (which coincides with life expectancy of our ancestors) is maybe to allow the mother time to rear the last child to puberty. This “protective mechanism” becomes an obstacle when it occurs early, in women who wish to delay birth. Until recently the only way to offset the consequences of ovarian aging was reverting to egg donation. In the last decade, an extension of the oncology related procedures of “fertility preservation” and the increasing efficacy of oocyte vitrification have fueled the imagination of patients and doctors to think that it is also the solution for all young fertile women or women with unproven fertility who delay marriage and birth to the fourth or fifth decade of life. Studies have proven that vitrified-thawed oocytes can fertilize at a high percentage, implant, and achieve normal pregnancies and offspring after a relatively “short period” of freezing (Rienzi et al., 2012; Cobo et al., 2013; COBO et al., 2014; Cobo et al., 2015; De Munk et al., 2016). Though, it is yet to be proven that oocytes frozen for a decade or more remain highly viable and effective, today's knowledge (Goldman et al., 2015) suggests that it will probably be the case even if the methods are still being refined in many clinics to reach the level of the published experience. At first sight, the issue seems straight forward. If done in a timely manner “social oocyte freezing” (SOF) can offer an efficient solution for women who opt to delay birth and can freeze the potential to conceive for a later age (Lockwood et al. 2011) A young woman who freezes her eggs before age 35 will freeze her potential to conceive during her fourth and fifth decades like her potential at the age of freezing. However, there are no studies supporting the cost-effectiveness of this practice- which is essentially offered to “fertile” or at the most to women of “unproven fertility”- who must undergo through costly, taxing, and somewhat risky IVF to preserve their potential. This is a new market for IVF clinic, one which is very profitable. No wonder that the idea stimulated also reservations and condemnation (ASRM 2009) which with time has unfoundedly partly subsided. Others (Radon et al., 2015) expressed the fear that the procedure will encourage patients to further delay birth. Doubts were also raised about the high efficacy of freezing (Kushnir et al 2015), these authors have found a lower live birth rate in donated eggs after freezing compare to fresh. Fertility preservation for social reasons is probably here to stay due not only to the logic behind it, but also the powerful marketing and patients-doctors interest. The offer to use freezing for social motives, is catching ground throughout the world, marketing a new indication that increases the request for IVF to the domain of fertile women. Nevertheless, SOF leaves many questions yet to be answered, apart from the need to frequently reassess the strengths, weaknesses and opportunities of the procedure, we need to redefine indication, and to evaluate the true cost effectiveness to the individual and to the society. SOF is a sort of insurance, where the full cost of the procedure must be paid upfront. Only those who have “bought” the full insurance “not too early and not too late” will have a chance of benefitting from its potential at a better cost. Early freezing is associated with higher success but lower usage percentage and lower cost effectiveness and vice versa. Also, differences in social practices like women who will attempt pregnancy only if married or after finding a known partner might be a barrier as age advances. While from medical perspectives, the women “buys” time and a sense of security, statistics shows that in

advance age the chances to accomplish the second condition i.e. getting married, are slim (Mesen et al. 2015). Hence, freezing and waiting to get married is contradicting, and proves detrimental to the chances of ever using the eggs and thus decreasing the cost effectiveness of the procedure. No wonder that some have dubbed SOF as buying a "lottery". SOF is a procedure without indication. The target population is all single women, at almost all age groups' certainly between 30-40 years. The users are affluent women for whom the cost might not be a prime issue, otherwise going through repeated cycles of egg banking might be too costly for most patients. Women who are trapped between the hammer of social changes and the anvil of aging ovaries are the target of aggressive marketing of this procedure by public and private clinics. Many are calling on governments or insurers to support large scale "fertility preservation" to offset the natural decrease in fertility, as well as to give a second chance to women who delay childbearing as if it is already a fully proven cost effective procedure. It is not surprising, therefore, that major global corporations like Apple and Facebook ([www.washingtonpost.com](http://www.washingtonpost.com), accessed Oct. 15<sup>th</sup>, 2014) have stepped in and have offered SOF as a "work benefit", which can allow young women to dedicate their prime years to their careers and delay birth without "worrying" about their future fertility. This highly publicized move came early during the course of the events, and perceived as endorsement to the technology from the "leaders of technology" and as the right move for young childless women adding to the conviction that freezing eggs is the right move for young affluent women, and before the medical community had the chance to appraise the full meaning of the procedure. But in theory a woman who freezes her eggs at 34 years and get married at 37, will most probably not use her frozen eggs first. She will first seek to be pregnant spontaneously, then with treatments and only if fails which is less than 5% of all women at that age, will use the frozen eggs, so a woman freezing her eggs at this age should know that she is paying the full cost with slim chances of utilization. The number of eggs needed to freeze at each age to give a fair chance of success differs and determine the cost. Statistics shows, that in general, only 1 of 20-25 eggs collected (4-5%) will result in the delivery of a baby (Doyle et al. 2016). The mean number of eggs collected in a single cycle is 8-12, which means that freezing of 20-25 mature eggs requires 2-4 cycles at a cost of 6-15,000 US\$ per cycle plus variable yearly storage cost. 20-25 eggs will allow 80-85% chance for a baby (Cobo et al. 2015); but after age 35, due to the decline in egg quality and quantity, a larger number of eggs are required to secure such a high success rate. Obviously, these figures are dependent on the male partner health and sperm quality which is unknown at the time of freezing. Therefore, the total financial commitment, be it for the individual or for the governmental budget, is enormous. Few theoretical studies tried to contend with the cost-effectiveness issue viv-a-vis the usage rate. Van Loendersloot et al (2011) have concluded that oocyte freezing is more cost effective than no freezing if at least 61% of women return to use their frozen eggs and are willing to pay 19,560 (cost of 6.5 cycles) Euro per live birth. The authors didn't comment if the goal of 61% usage rate is at all achievable. Others (Devine et al., 2015) have concluded that oocyte cryopreservation remained cost effective as long as performed before age 38 years, and if more than 49% of those women not obtaining live birth spontaneously returned to thaw oocytes. It is noteworthy that also these authors stressed the point of "percent usage" as a major factor in determining the

cost benefit calculations, these authors also didn't comment however, if such a high usage rate (49%) is realistic and achievable. Interestingly, Devine et al have set the age higher (<38 years) than the clinical suggestion (30-35 years) and similar to the real-life results (Cobo et al., 2016, Hammarberg et al., 2017). Also, since the cost of IVF varies widely (2-6 fold) between countries and between the studies that originated in the USA and Europe, prices should be compared as multiples of the cost of single IVF cycle for each country. Another study (Hirschfeld Cytron et al., 2012) performed calculations based on 3 different strategies examining the cost per live birth: They concluded that in their model of freezing at 25 and use the frozen eggs or frozen ovarian tissue at 40 years after 6 cycles of conventional treatment, both freezing strategies did not appear to be cost-effective when compared to the waiting strategy. Mesen et al (Mesen et al., 2015) have constructed a theoretical model for women ages 25 to 40 attempting conception 3, 5, and 7 years after freezing with or without electing to marry before usage. They found that oocytes cryopreservation was most cost-effective at age 37, at a cost of \$28,759 per each additional live birth. Little benefit over no action was seen at ages 25-30 years (2.6%-7.1% increase). Moreover, if the probability of getting married was factored-in, as many women were ready to use the eggs only if they will get married, cryopreservation resulted in no improvement in live birth rates. The societal cost for additional live birth between ages 25-30 in such case will sky-rocket to an incredible cost of \$366,824-\$698,722, casting doubts over early freezing strategy for the individual and surely for the society. If the societal cost is dependent on usage rate, what is the maximal usage rate that can be expected? Can we reach the about 50% needed to make SOF cost effective? The answer is no! (table 1) It is widely accepted that about 10-15% of all couples between the ages of 25 and 35 are infertile, gradually growing to 35-40% after 35, and reaching over 50-60% infertility after 40. We have used the data from a recent large study (Malchau et al 2017) on 19,884 women to assess the realistic usage rate possible in each age group. These authors have shown that the cumulative delivery rate (treatment dependent and independent) of 80%, 60% and 26% respectively was achieved within 5 years in these 3 age groups respectively this despite an annual fertility rate drops at each age group of 4% <35, about 15% between 35-39, and 33% ≥40 by respectively. Combining these two sets of numbers (table 1) provides the answer. Of the maximal 15% infertile women under the age 35 years, 80% will achieve pregnancy with or without treatment leaving only 3% infertile. This represent the maximal "usage rate" for this age group if all the group would freeze eggs, a figure which is extremely non-cost effective. At the age group of 35-39, of the maximal 40% infertile women, 60% per Malchau et al, are expected to succeed leaving only 24% infertile or less, which represent also the maximal expected usage rate at this age group if all of them would freeze eggs and be ready to use them. In the age group of ≥40, (an age at which most doctors will not suggest freezing) of the about 60% infertility rate, only 24% are expected to be successful, and 45% remained infertile. Since the mean age for egg banking is above 37 years they are not supposed to come closer to the expected utilization rate and this, without factoring the women who are opting to get married first, which drop the usage rate even further. An unexpected support to this calculation were provided recently from real-life studies evaluating the usage percentage and the age at egg banking. (table 2) The first study (Cobo et al., 2016) shows that from 1468 women freezing their eggs,

between 2007-2015, at a mean age of >37 years only 137 (9.3%) returned to use their oocytes and only 40 babies were born (2.7% per patient) which concurs with the theoretical estimation, and is far lower than the minimum usage of 50-60% that was calculated to be cost effective. If we put a modest tag price of \$8,000 per cycle and considering only two such cycles for egg collection and storage than the cost for each baby born in this study reaches about 600,000 \$ ( $1,468 \times 8,000 \times 2 : 40$ ). Per the second study (Hammarberg et al., 2017) of 193 women who stored their eggs between 1999-2014, the mean age at the time of freezing was like the previous study >37 years (range: 27–42) and the average number of oocytes stored was 14.2. 18 patients conceived spontaneously or with treatment, only six women (3.1%) returned to use the frozen eggs and 3 patients got pregnant (1.5%). Assuming again a cost of \$8,000 per cycles and two cycles per patients, the societal cost per live birth was >\$ 1,000,000. While one in three women got pregnant at some stage without the frozen eggs, the main reason stated for not using stored oocytes was not-wanting to be a single parent. The low usage percentage commensurate with our calculation and the high societal price per live birth (of about \$600,000-1000,000) is probably an underestimated, since many will need >3 cycles and the cost-plus storage in many countries might be higher. In both studies, the age of freezing was >37 years, higher than advice by most physicians, but it seems that the public wisdom perceived what we Doctors might have missed, with our good intentions to help. The mean age of freezing is not surprising considering the high cost and low overall efficacy of egg banking, and the hope to succeed without medical help! At this age, at which cost effectiveness becomes a bit better (Mesen et al 2015), the success rate is not more than 30% with 10 metaphase II oocytes which translate to over 30 eggs for 85-90%. This led the authors to suggest that patients should come at earlier age (Cobo et al 2016), which we will only make SOF less cost-effective. To increase the chances of future usage of frozen eggs and make the all procedure more cost effective, we should have more strict indications which will decrease the denominator, but SOF has no clear indication. For example, women who are destined to be poor responders and who have up to 100-fold less eggs at any given age than other women could have been the prime indication. These women are the first to pay the price of the current social practice to delay childbearing. If we could identify them before they become low responders, we could offer them a thorough consultation including SOF to protect their fertility or allow them time to better space childbearing. However, the currently used tests - like antral follicular count, anti-mullerian hormone and FSH levels - can identify poor ovarian reserve only when it started (Broekmans et al., 2007) and the patients are already low producers of eggs. The lack of tests capable of predicting low response ahead of time is a great limitation in our ability to serve these patients with egg banking when the cost and effectiveness can be higher. Another possible target group are women with endometriosis who must go through an endometrioma operation. It is well recognized that such an operation may decrease the ovarian reserve and, therefore, must be delayed if possible. However, if such an operation is deemed necessary, it is important to consider freezing eggs before the operation in case the patient loses ovarian potential and becomes low responders (Somigliana et al., 2015). The publication by Malchau, indicates that the adjusted annual odds ratio for birth in smokers and women with BMI>30 may be 7% , faster than usual annual 1-4% and if confirmed they

may be another indication to offer SOF earlier. Other rare genetic or chromosomal anomalies that are associated with premature menopause (like Mosaic Turner Syndrome or fragile X) or BRCA carrier that might need early oophorectomy are legitimate candidate for early egg banking but do not fall under this discussion. In conclusion, As IVF treatments move from the public sectors to private hands, it is not easy even for the expert to decipher the scientific claims from the business-oriented claims. The fact that the sales agent of SOF are the same doctors who carry out the procedure and benefit financially carries a potential conflict. SOF is a new option for IVF-units to offer their services to supposedly perfectly fertile women who are offered to "hedge" fertility by diversifying their future options. The procedure is growing in popularity; however, the literature on the true effectiveness of this procedure is only now starting to accumulate, and its seems too low to make it cost-effective for the society. Moreover, also for the individuals who as to bear the full costs, freezing might not be a panacea. Despite being urged to freeze at young age, patients probably perceive the contradiction between egg banking at early age, when the success might be high but utilization and cost effectiveness is expected to be low, and freezing at later age and so the mean age of freezing is above 37 years – which seem suboptimal but contra-intuitively - the results can be a bit more cost-effective (Mesen et al., 2015). The pregnancy rates in these studies for the few cases that returned to use their eggs was high, but the overall usage rate extremely low (Cobo et al., 2016, Hammarberg et al., 2017), and the cost per viable birth becomes disturbingly high to level that might deter even affluent individuals if consulted properly. One of the leading reasons of the low usage is the high chances of success in mothering a child spontaneously or by various treatments including IVF before age 39 (Malchau et al. 2017). Most women who opt for single parent family with sperm donation, have a high chance to achieve motherhood also between 35-39 without freezing eggs. Obviously, women who accept to use sperm donation can just try as soon as possible and need not to freeze eggs. If the patient had frozen eggs early and decide to conceive she will exhaust other treatment before she uses the stored eggs hence usage will be low. On the contrary, women who are planning to use the stored eggs only if they will have a partner, should know that the chances to achieve this second condition is low and accordingly, the chances to use the eggs are very low which makes freezing non-cost-effective. (Mesen TB et al, 2015; Hammarberg et al., 2017) **In summary:** Except for few rare genetic associated indications, we are lacking real indications and reliable methods to predict who will benefit from cost-effective SOF later in life. Nevertheless, it is important to frequently refresh the cost benefit and cost efficacy calculations based on real results and present to the patients and the public clear and trustful information including the low numbers returning to use the eggs and the reasons. Presenting the correct statistics and the alternative options, is in everyone's interest. Women should know about the decrease in fertility after age 39, about the low statistical chances to find a partner after that age, about the chances to conceive spontaneously or with treatments before using the frozen eggs and about the advantages and disadvantages of SOF, including the chance that the frozen eggs may never be used, and the option of egg donation as a cost-effective alternative. Recent suggestion that preservation of autologous ovarian tissue and re-implantation at later age can be the "HRT of the future", should be met with similar criticism that was raised here.

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Table 1: Theoretical calculation of the maximal "Usage percentage" that can be expected for each age group after using results from Malchau SS et al 2017

Age	AOR*	% infertile	% Pregnant Spont.	% Pregnant With treatment	Cumulative pregnant	Overall % Not pregnant**
26-35	4%	15%	16%	64%	80%	3%
35-39	15%	40%	10%	50%	60%	24%
>40	33%	60%	11%	16%	26%	45%

\*AOR-Annual Drop in Adjusted odds ratio for live birth rate with age

\*\* calculation of the maximal possible usage rate expected if entire age-group will freeze and all will opt to use the banked eggs after treatment failure.

Table 2 : Cost of each new delivery, assuming cost per egg retrieval plus storage of \$8000, and assuming only one or two cycles of freezing per patient. Note the usage rate is below 10%.

	Cost per cycle	Years	No of pt freezing	Mean age	Returned to use	Pregnant	Cost per each baby	Conceived spontaneously
COBO 2016	One cycle - \$8000	2007-2015	1468	>37	137 (9.3%)	40 (2.7%)	293,600 \$	?
	2-cycles \$16,000						About \$600,000	
Hammberg 2017	One cycle - \$8000	1999-2014	193	>37	6 (3.1%)	3 (1.5%)	514,666 \$	18*
	2-cycles \$16,000						\$1,000,000	

\*18 patients conceived spontaneously compare to 3 with banked eggs

## OPTIMIZING PSYCHOSEXUAL HEALTH WITH PERIMENOPAUSAL CONTRACEPTION

Johannes Bitzer, Switzerland

Psychosexual health and wellbeing is an important part of the quality of life.

Psychosexual health in perimenopausal women has shown to be impaired in different dimensions

- Depressive mood and mood instability, depressive episodes, major depression
- Situational anxiety and anxiety disorders
- Body image disorders
- Eating disorders
- Increase in sexual dysfunctions ( Low desire, arousal and orgasmic disorder, pain disorder)

The objective of contraception in this life phase is to provide effective protection against an unwanted pregnancy, low health risks, good tolerability but also if possible to improve quality of life including psychosexual health. So the question arises: What is the best method for a perimenopausal woman with sexual pain, low desire, depressed and anxious mood, heavy menstrual irregular bleeding?

The answers to this question will be discussed

## SHOULD ANDROGENS BE ROUTINELY OFFERED TO OPTIMIZE QUALITY OF LIFE IN MENOPAUSE

Johannes Bitzer, Switzerland

Androgens are essential hormones for women's health. In many women there is a decline in androgen levels starting about in the middle of the third decade. Knowing that androgens may play a role in bone health, mental health, sexual health the question arises whether this age related

decline in the body's production should be compensated for by routinely providing women with androgen taking into account possible side effects and risks **The evidence base answers are:** There is no evidence that androgen replacement in peri and postmenopausal women improves mental health, bone health, general wellbeing. There is good evidence that androgen replacement therapy which restores premenopausal values of testosterone improves sexual function in postmenopausal but not in perimenopausal women. There is good evidence that this type of therapy has major health risks and no or only minor side effects (skin) **The conclusion:** There is no evidence that androgens should be routinely offered to women after menopause. Instead there is a place for testosterone therapy for desire disorder in combination with psychosexual therapy.

#### PRENATAL AND POSTNATAL EXPOSURE TO ENDOCRINE DISRUPTING CHEMICALS AND MALE REPRODUCTIVE DISORDERS

Jens Peter Bonde MD and Sandra Søgaard Tøttenborg PhD  
Bispebjerg and Frederiksberg Hospital and University of Copenhagen, Copenhagen, Denmark

It is undisputed that high-level occupational exposure to xenobiotic chemicals may impair testicular function and fertility of the adult male. Since the reporting of devastating and in some cases long-lasting effects on sperm counts conferred by exposure to the nematocide dibromochloropropane (DBCP) in production and agricultural workers in 1977, strong evidence on adverse effects of several other occupational hazards to male fecundity has accumulated. These include other pesticides such as ethylenedibromide and carbaryl, organic solvents as some ethylene glycol ethers, welding of metals even though the causative agents remains elusive, inorganic lead at levels far above background levels, ionizing radiation, and radiant heat. The hypothesis that endocrine disruption of the fetal programming of the testicles may result in reduced sperm count and infertility in adulthood has since the 90's shifted focus from occupational exposures in adulthood to exposures prior to conception and during prenatal life. The endocrine disruption hypothesis is based on the pivotal role of sexual hormones during development of the fetal testes (1). It has been demonstrated that numerous environmental chemicals - including some of those earlier recognised as occupational male reproductive toxicants e.g. inorganic lead - have weak endocrine activity *in-vitro* and *in-vivo* with the potential to disrupt endogenous hormone signaling. Meanwhile persistent as well as fast metabolised chemicals such as DDT, PCB, and phthalates, detected in the bodies of almost everyone all over the globe, cause male reproductive anomalies in rodents. Add to this reports on dramatic secular trends of male reproductive disorders, studies indicating synergistic effects of concurrent exposure to chemicals, and arguments that challenges the toxicological paradigm of monotonic dose-response effects, the scene is set for great scientific as well as public awareness and concern. Nevertheless, the potential environmental impact on male reproductive health due to endocrine disruption of fetal development is a controversial topic that divides the scientific community. Opponents argue that claims of declining sperm counts during the past half century are not based upon solid evidence and inconsistent with the best population-based prospective studies, that diethylstilbestrol as proof of concept of the estrogen hypothesis is flawed, that adverse effects of chemicals with very low potency at extremely low levels are implausible, and that the claim of synergistic effects ignores results of large high-quality epidemiological studies addressing mixed exposures. This ongoing controversy calls

for systematic and transparent reviews of current epidemiological evidence according to international guidelines. Only one such systematic review that explicitly addressed prenatal exposure to endocrine disrupting chemicals and risk of male reproductive disorders has to the best of our knowledge been published (2). In 2018 we identified altogether 33 epidemiological studies with 85 risk estimates reporting associations between male reproductive disorders and exposure to endocrine disruptors documented by biochemical analyses of biospecimens. The overall odds risk ratio across all exposures (four different classes of endocrine disrupting chemicals) and outcomes (low sperm counts, hypospadias, cryptorchidism, and testicular cancer) was 1.11 (95% CI 0.91-1.35). **In conclusion**, findings so far do not indicate strong prenatal effects of environmental chemicals classified as endocrine disruptors, but it is important to acknowledge that the evidence base is limited. In particular data on semen quality are sparse. With few exceptions, however, the hypothesis has been impossible to test in epidemiological studies as appropriate prospective data on time-specific exposures combined with clinical follow-up of sons two decades later when they reach adulthood have been lacking. A new large male-offspring cohort - the Fetal Programming of Semen Quality (FEPOS) cohort (3) - serves an unprecedented chance to finally put the hypothesis to a critical test, and future epidemiological studies may change the weight of the evidence in either direction.

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#### 1ST TRIMESTER ULTRASOUND SCREENING

Rabih Chaoui

Fetal Diagnosis and Human Genetics Center - Berlin-Friedrichstrasse 147, 10117-Berlin, Germany

In the early and mid 1990ies a new ultrasound screening policy was introduced by K.N. Nicolaides as a first trimester screening for the measurement of the fluid behind the neck, called nuchal translucency (NT). The NT screening was completed by biochemistry values to achieve a risk assessment for the presence of common aneuploidies as trisomy 21, 18 and 13. In the last decade however there was an increased uptake of the new cell-free DNA screening for aneuploidy in maternal blood with a high sensitivity and specificity. With the advent of high-resolution transducers in the past two decades, the first trimester NT ultrasound examination has evolved beyond aneuploidy screening and now includes an evaluation of fetal anatomy in early gestation. International and local released guidelines reflect this development. In addition, the measurement of Doppler of the uterine arteries allows along with biochemistry values to assess the risk for preeclampsia. The presentation will focus mainly on the NT screening, the diagnosis of obvious findings in the first trimester and the role of a protocol in the systematic evaluation of the fetus to diagnose anomalies of the CNS, the heart and other organs. First trimester screening should no longer be considered as a solely aneuploidy screening but has evolved to be a screening tool for complex anomalies between 11 and 14 weeks of gestation. This however should be followed by a second trimester screening, as some anomalies evolve and some develop between the first and

second trimester.

## Er:YAG VAGINAL LASER THERAPY - HYPE OR ESTABLISHED TREATMENT?

Ivan Fistončić

*Institute for Women's Health, Zagreb, Croatia*

Noninvasive treatment is recommended as first line for urinary incontinence (UI) in women. However, surgical procedures are more likely to be implemented to cure UI but are associated with more adverse events. Less invasive operative mesh techniques are relatively effective, but not immune to complications such as bleeding, bladder perforation, urethral injury, infection, and the retention requiring mesh resection. In patients for whom the risks of anesthesia and surgery are too high, a minimally invasive approach is recommended and further research is needed in terms of more compliant, less invasive and low-cost methods for the treatment of stress UI and pelvic floor dysfunction. Contemporary scientific and technological breakthroughs have led to better clinical outcomes with minimally invasive procedures with shorter recovery times and lower implicated costs. In this sense, recent evidence supports laser treatment as an effective and compliant intervention for stress UI. Although laser is an attractive novel, non-hormonal new technology for the treatment of the GSM, additional studies are needed to explore the long-term safety and efficacy of various laser therapies for genitourinary symptoms. Non-ablative, thermal-only SMOOTH®-mode erbium YAG laser pulses are used to produce vaginal collagen hyperthermia, followed by collagen remodeling and the synthesis of new collagen fibers, resulting in improved vaginal tissue tightness and elasticity. Evidence has shown that the intravaginal laser improves vaginal elasticity, pH, discharge, mucosal integrity, and moisture reducing vaginal dryness, dyspareunia, itching, burning and dysuria, providing an increase in sexual gratification. Biopsies have shown a thicker epithelium and improved maturation index increasing the ratio of parabasal, intermediate, and superficial cells showing an estrogenic effect. Breast cancer survivors, especially at younger age, frequently face serious difficulties in their sexuality due to GSM. Laser thermotherapy has shown high level of effectiveness in those who are not able to use local hormonal therapy. Growing evidence supports non-ablative laser technology as an effective intervention for stress urinary incontinence, vulvo-vaginal atrophy, lichen sclerosus atrophicus, overactive bladder, vaginal relaxation, etc. Despite of warnings from leading international organizations against the use of energy-based devices (EBDs) in certain fields of gynecology, contemporary evidence confirm safety and efficacy of laser treatment for genitourinary syndrome of menopause (GSM). Future studies need to be designed taking mentioned considerations into account, including the histological assessment performed immediately after treatment that will help compare morphology at baseline with changes in the vaginal architecture following laser procedure. Next studies should focus on the individual patient level in order to predict personal risk or benefit based on the decision of undergoing a given proposed procedure. Simultaneously, predictive systems may impact public health policies in terms of prevention. In spite of promising initial results, there is still need for long term consistent evidence analyzing laser efficacy and safety in the treatment of female UI. **Keywords:** *erbium YAG laser SMOOTH®, urinary incontinence, minimally invasive treatment*

## ULTRASOUND IN THE DELIVERY ROOM

Tullio Ghi, *Italy*

The assessment and management of a woman in labor is traditionally based upon clinical examination. The diagnosis of labor arrest and the timing of interventions rely on the digital evaluation of cervical dilatation and effacement, fetal head station and position. However, clinical examinations of station and position are inaccurate and subjective, especially when a caput succedaneum impairs palpation of the sutures and fontanels. The use of ultrasound has been proposed as an aid in the management of labor. Several studies have demonstrated that ultrasound examinations are more accurate and reproducible than clinical examinations in the diagnosis of fetal head position and station and in the prediction of labor arrest. Ultrasound examination in labor can to some extent, predict which laboring women in the second stage are destined for spontaneous vaginal delivery or operative delivery. Finally, there is growing evidence that US in labor may predict the outcome of instrumental vaginal delivery. Ultrasound in labor can be done transabdominally, mainly for head position and spine position or transperineally (TP) for assessment of head station and position at low stations. Several quantitative sonographic parameters have been proposed to assess head station. Recently the guidelines on the appropriate use of labor ultrasound have been published by the International Society of Ultrasound in Obstetrics and Gynecology. In this document it is recommended when ultrasound should be performed in labor, which parameter(s) should be obtained and how the sonographic findings should be integrated in the clinical practice in order to improve the management of the patient.

## ACUTE ABDOMEN DURING PREGNANCY

Wolfgang Henrich

*Direktor der Klinik für Geburtsmedizin, Director of the Department of Obstetrics, Campus Virchow Klinikum, Campus Mitte, Charité - Universitätsmedizin Berlin, Charité - University Medical Center Berlin, Augustenburger Platz 1 / Charitéplatz 1, 13353 Berlin / 10117 Berlin, Germany*

Abdominal pain is a common symptom in nonpregnant and pregnant women and may have a variety of reasons. It often presents a diagnostic dilemma. Nausea, vomiting and mild abdominal pain are common symptoms in intact normal pregnancies, but they could also be the first signs of relevant severe disease. Physical examination in pregnancy is limited and more difficult due to the enlarged pregnant uterus and the displacement of other organs, depending on the gestational age. Acute abdominal emergencies occur in pregnant women with the rate of 1:500. These conditions usually develop acutely from a normal clinical status and worsen rapidly. The history of the patient, presence of previous operations, the quality and point of maximum of the pain are helpful in distinguishing possible reasons. The abdominal wall is distended, and a peritonitis can be mild. The leukocyte count is of limited information because of a physiological increase in leukocytes in pregnancy. The differential diagnosis is therefore difficult, and both the mother and her child are at risk. Delayed treatment could harm both, on the other hand overtreatment increases the risk of prematurity and operative complications. Fast abdominal ultrasound is the initial tool to distinguish between non-obstetrical etiologies and more common obstetrical reasons like abruption of placenta, uterine scar dehiscence or rupture, uterine hyperstimulation, uterine torsion or sacculation. After the sonographic evaluation of the fetus, the uterine wall, the placenta, the amniotic fluid and cervical length, free fluid in the abdomen should be excluded (perihepatic, paracolic and in the Morrison

pouch as well as in the Pouch of Douglas). Free fluid is common after ruptured ovarian cysts or perforated gastric ulcer. Generally acute abdomen occurs in appendicitis, small bowel obstruction due to adhesions or volvulus, acute inflammatory bowel disease, acute cholecystitis and pancreatitis, gastric ulceration, adnexal torsion, necrotizing fibroma, abdominal wall or diaphragmatic hernia, splenic rupture, abdominal trauma, urological problems e.g. urolithiasis, acute hemoperitoneum after spontaneous rupture of vessels and very rarely in pseudoaneurysms of arteries. Gallstones can be visualized in the gallbladder directly and by stone shadowing. Cholecystitis can be associated with pancreatitis and classical laboratory parameter changes. Small bowel obstruction e.g. by adhesions (in the majority of cases after appendectomy), are visible by dilated intestinal loops without peristalsis or swinging peristalsis. In case of urolithiasis, the stones can be sometimes directly visualized, indirect signs are hematuria and a dilated renal pelvis and colicky pain. Perforated gastric ulcer can occur after the application or overtreatment with nonsteroidal antiphlogistic pain medication. Noncontrast magnetic resonance imaging is increasingly used as an imaging mode to evaluate pregnant women with abdominal pain, either as the first-line test or as a second diagnostic test following ultrasonography. A case series of patients with different reasons for an acute abdomen and the management will be discussed in the lecture.

## ULTRASOUND IN THE POST PARTUM PERIOD

**Wolfgang Henrich**

*Direktor der Klinik für Geburtsgynäkologie, Director of the Department of Obstetrics, Campus Virchow Klinikum, Campus Mitte, Charité - Universitätsmedizin Berlin, Charité - University Medical Center Berlin, Augustenburger Platz 1 / Charitéplatz 1, 13353 Berlin / 10117 Berlin, Germany*

Postpartum Sonography (PS) complements the clinical examination, ideally for rapid clarification of either a pathological placental period, bleeding sources or birth injuries. The use of mobile ultrasound equipment in the delivery room or on the post-delivery ward allows often quickly to achieve the correct diagnosis. In placental retention, the placenta is not born within 30 to 60 minutes. It is the second most common cause of postpartum hemorrhage (PPH) after uterine atony. A completely or partially separated placenta impairs uterine contraction and often leads to increased bleeding. In such cases, the placenta must be separated manually or removed instrumentally, preferably with ultrasound guidance. The sonographic surveillance during such procedures reduces the risk of complications, e.g. of a perforation or the uterus. Both B-scan imaging and color Doppler sonography of the placenta can help to evaluate the myometrial thickness and placental bed to rule out an abnormally invasive placentation. The absence of the "separation sign" and the persistence of blood flow between the myometrium and placenta in Color Doppler may be an indicator of abnormally invasive placenta (AIP, Placenta accreta, increta or percreta). In some cases, the patient may benefit from ultrasound-guided curettage to selectively remove cotyledons implanted at a deeper focal area, and in other cases, to act cautiously in the case of AIP with thin myometrium and the threat of an instrumental perforation. Cotyledons cannot always be distinguished from clotted blood or a submucous myoma by B-mode US alone. The visualization of blood perfusion in an intracavitary mass by Color Doppler is mostly a sign of placental remnants. Increased blood flow to the myometrium in the area of the adherent placental residua is typical, but absent in clots and in older or detached avital placental tissue. Increased vaginal bleeding after a caesarean section in the puerperium can also

indicate placental remnants. After manual or instrumental removal of the placenta or placental remnants, the sonographically empty cavity of the uterus can be documented with a still image. Retained clotted blood after a primary c-section and a closed cervical canal can lead to pain and delayed involution of the uterus. Dilatation of the cervical canal can be performed without curettage to empty the uterine cavity. In the case of uterotonics-resistant atony, which often occurs after manual and instrumental emptying of the cavity, the insertion of an intrauterine chitosan tamponade or of a balloon has proven to be effective. The correct position of the tamponade or balloon can be confirmed sonographically. A secondary accumulation of blood in the cavity can also be detected. Postpartum and post-operatively, abdominal sonography is also helpful to detect hematomas, to determine their size and to rule out a hemoperitoneum in the case of uterine rupture. Uterine compression sutures are used as an alternative to a tamponade in cases of persistent bleeding during a c-section. These sutures can be visualized by ultrasound and followed up in the postoperative course weeks later. Arterio-venous malformations (AVM) or pseudo-aneurysms are rare differential diagnosis of pathologic postpartum uterine bleeding. They occur after endo-uterine trauma (surgery) or are, rarely, congenital. They may occasionally become symptomatic postpartum for the first time. The main symptom is bleeding. Sometimes they are accidental findings during routine follow-up. Correctly diagnosing a symptomatic AVM or pseudo-aneurysm is essential to avoid the accidental provocation of increased bleeding during an attempted curettage. Radiological interventional embolization is the therapy of choice for symptomatic bleeding in AVM or pseudo-aneurysm patients. Surgical interventions are usually not necessary and required only in hemodynamically unstable patients who cannot be treated with radiological interventional therapy. Abdominal hematomas or seromas, as well as pre-uterine hematomas can be diagnosed by abdominal and/or vaginal sonography. Size, echogenicity and the dynamic aspect may indicate whether a hematoma is fluid and suitable for drainage by puncture or inhomogeneous and clotted. An edematous border indicates an infected hematoma. Hematomas between the lower uterine segment and the bladder wall are rarely found after caesarean sections, as the visceral peritoneum nowadays usually does not get sutured. However, increased uterine bleeding from the uterine suture can lead to a hemoperitoneum, which can be visualized in ultrasound as a free fluid, mixed with blood clots. A case series with the use of postpartum ultrasound and management strategies of pathological findings will be discussed in the lecture.

## IS LASER FIRST LINE TREATMENT FOR THE MANAGEMENT OF GSM? – NO!

**Tim Hillard**

*Consultant Gynaecologist, University Hospitals Dorset, Poole, UK*

GSM is a debilitating condition that affects the lives of millions of post-menopausal women. The central underlying problem is vulvo-vaginal atrophy that stems from loss of estrogen after the menopause. Despite widespread publicity over recent years, lack of awareness and recognition of the problem by both women themselves and their health care professionals remains the biggest challenge to successful management. Of the existing treatments, vaginal estrogen is the current gold standard and recommended by all relevant international societies. Whilst there may be increasing evidence that vaginal laser can be effective in alleviating the symptoms of GSM, the time is not right for it to become first line therapy.

The evidence base for vaginal laser is growing but many of the studies are uncontrolled, of short duration and with low numbers. Efficacy after 3 treatments seems to wear off after around 18 months and requires additional treatment sessions. In the clinical studies the procedures seem well tolerated with minimal side-effects and no reported long-term sequelae. However there remains a genuine and justifiable concern that repeated thermal injury to the vaginal epithelium may lead to scarring and longer-term problems such as vaginal pain. Longer and more robust follow up data are needed before this can be answered. There are many unanswered questions around vaginal laser therapy and where it fits in our clinical practice. Not all vaginal lasers are the same and any recommendations need to differentiate between those that have compiled appropriate data and those that have not. There is an urgent need to have standardisation of the technique and the procedure with mandatory outcome data recorded. There should also be clear guidelines on training and overall governance of these procedures which should be performed by appropriately trained health care professionals who have a full understanding of the various options available.

#### US EXTERNAL VERSION IN BREECH PRESENTATION Larry Hinkson, Germany

Cesarean Sections are on the rise with the global average rate of 19.4%. The external cephalic version (ECV) is a recommended low-risk, non-invasive intervention to manage women in pregnancy with a breech baby from the 36th week of pregnancy and is recommended by international societies to improve the likelihood of vaginal delivery and reduce the rising rate of cesarean sections. The incidence of breech presentation is reported to be at 5 % of all pregnancies at term and the ECV is recommended in these cases by both the American College of Obstetricians and Gynecologists and the Royal College of Obstetricians and Gynecologists in the UK to reduce cesarean sections. The success rate of this intervention is however between 35-86% and therefore quite variable. We investigated the success rate of ECV in our obstetric clinic and determined favorable sonographic criteria associated with a successful attempt. These results will allow doctors to better advise patients on the chances of success and to identify favorable and unfavorable parameters so that patients can make better informed decisions. All ECVs are performed with sonographic support and with the ECV recorded live sonographically. Sonographic parameters include the documentation of triggered fetal reflexes (Galant Reflex and the Stepping Reflex ) described by our research group (Hinkson et al) as an aid to external cephalic version. Twin pregnancy is also an increasing indication for cesarean section. Normally, a twin pregnancy with a non-cephalic presentation of Twin A is routinely scheduled for cesarean section in up to 92% of cases. Whilst the external cephalic version (ECV) is a recommendation for singleton pregnancies, there is a paucity in the literature on the consideration of this option prenatally in twin pregnancies where twin A is in breech. We demonstrate a technique where it was possible to perform electively an ECV on a breech twin A giving the mother the option of vaginal delivery. We found this procedure to be effective in the 36th week of pregnancy. A detailed sonographic examination to identify the location and orientation of the separating chorioamniotic membrane, growth parameters, liquor volume, placenta location, umbilical cord location and position and orientation of both twins is essential in planning the ECV. Tocolysis is avoided. The ECV of the breech twin A is performed with the patient lying on the side avoiding aorto-caval compression and affording more

surface area access for palpation of the leading twin. Promoting safe vaginal delivery in twins is important in reducing the high cesarean section rates. ECV for twin A in breech is possible and can avoid cesarean sections in this group.

#### EFFECTS OF A THREE-COMPONENT LIFESTYLE PROGRAM ON WEIGHT LOSS IN WOMEN WITH PCOS

\*Geranne Jiskoot, MSc.<sup>A,B</sup>, Reinier Timman, Ph.D.<sup>B</sup>, Annemerle Beerthuisen, Ph.D.<sup>B</sup>, Alexandra Dietz de Loos, M.D.<sup>A</sup>, Jan Busschbach, Ph.D.<sup>B</sup> and Joop Laven, M.D., Ph.D.<sup>A</sup>  
<sup>A</sup> Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology and <sup>B</sup> Department of Psychiatry, Section Medical Psychology and Psychotherapy, Erasmus MC, Rotterdam, The Netherlands

**Problem statement:** The prevalence of overweight and obesity is significantly higher in women diagnosed with Polycystic Ovary Syndrome (PCOS) compared to women without PCOS. Most women with PCOS suffer from overweight and obesity throughout their entire lifespan. Obesity worsens the reproductive, metabolic and psychological symptoms of PCOS. Weight loss can improve psychological symptoms (depression, anxiety, quality of life), reproductive function (menstrual cyclicity, ovulation and fertility) and metabolic symptoms (insulin resistance and risk factors for cardiovascular disease and type 2 diabetes mellitus), even when weight remained in the overweight or obese range. Therefore, multidisciplinary intervention are the first-line treatment for weight loss in women with PCOS. Although it is not clear whether lifestyle interventions are effective in the long-term. Three-component lifestyle interventions (LS) combining nutritional advice, exercise and cognitive behavioral therapy (CBT) have not been tested in long-term interventions in this group of women. **Methods:** We performed a longitudinal randomized controlled trial (RCT) measuring the effectiveness of a three-component multidisciplinary 1-year lifestyle intervention program in women with PCOS. The Medical Research Ethics Committee of the Erasmus MC in Rotterdam approved this study (reference number MEC 2008-337). This study was registered at the Dutch trial register by number NTR2450. We conducted the study at the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology of the Erasmus MC, Rotterdam, the Netherlands. Women were eligible if they: 1) were diagnosed with PCOS according to the Rotterdam 2003 consensus criteria; 2) had a BMI above 25 kg/m<sup>2</sup>; 3) were between 18 and 38 years old; and 4) wished to become pregnant. Participants were assigned to either one year of: 1) 20 group sessions of cognitive behavioral therapy, nutritional advice and exercise (LS without SMS) 2) 20 group sessions of cognitive behavioral therapy, nutritional advice and exercise with additional 9 months electronic feedback through SMS via their mobile phone (LS with SMS) or 3) care as usual (CAU). The 1-year multidisciplinary LS intervention consisted of 20 CBT group sessions of 2.5 hours over the course of one year. Important principles and techniques of the CBT component were self-monitoring, realistic and achievable goal setting, developing new coping skills to handle or prevent relapses and promotion of alternative behaviors during critical emotional situations or negative mood states. In addition, cognitive restructuring was used for challenging dysfunctional eating, body-related beliefs, and schemas by using thought records. The primary aim of this study was to test whether the LS was more effective to decrease weight compared to CAU. In addition, whether LS with additional SMS was more effective than LS without additional SMS to decrease weight. **Results:** Between 2010 and 2016, 209 women provided written informed consent, of

whom 26 were included in the pilot study. At baseline, 63 participants were randomized to LS without SMS; 60 to LS with SMS and 60 to CAU. A total of 183 participants were available for the intention-to-treat analyses and 487 measurements were used for the analyses. The mean weight loss was 2.32 kg in CAU, 4.65 kg in LS without SMS and 7.87 kg in LS with SMS. The difference in weight loss between the LS and CAU was 3.7 kg in favor of the LS ( $P < 0.001$ ). If we compared LS with SMS to LS without SMS we observed 3.2 kg more weight loss in LS with additional SMS ( $P = 0.017$ ). The effect sizes of the intervention (expressed in Cohen's  $d$ ) were very small in CAU ( $d = -0.16$ ), small in LS without SMS ( $d = -0.32$ ), and medium in LS with SMS ( $d = -0.55$ ). In CAU, 21.8% of the women had a weight reduction of more than 5% compared to 52.8% of the women in LS without SMS and 85.7% in LS with SMS. The odds ratio of achieving a 5% weight loss was 7.0 ( $P < 0.001$ ) in LS compared to CAU. The difference between LS with or without SMS was not significant ( $P = 0.130$ ). A 10% weight loss was achieved in 6.8% of the women in CAU and in 23.7% of the women in LS. This difference was not significant ( $P = 0.100$ ). Weight gain was observed in 29% of the women in CAU, versus 8.5% in LS without SMS and 3.1% in LS with SMS. The odds ratio to gain weight was 6.2 ( $P = 0.021$ ) for LS compared to CAU, in favor of LS. The overall dropout rate was 116/183=63.4%.

**Conclusion:** Overall, we conclude that a group-based three-component lifestyle program that combined nutritional advice, exercise and cognitive behavioral therapy resulted in reasonable weight loss in women with obesity and PCOS. Additional tailored SMS feedback seems useful to remind, encourage and motivate participants in the lifestyle intervention and increased the odds of achieving weight loss.

#### KISS-PEPTIN; PROMISE BECOMES THE STANDARD?

**Cornelis B. (Nils) Lambalk**

*Department of Obstetrics and Gynaecology,  
Amsterdam University Medical Centers, Amsterdam, The Netherlands*

The start of the successful clinical era of kisspeptin and its related neuropeptides reads like a one thousand and one nights fairy tale in the way its receptor was discovered in a large Arab family and published in 2003 in the *New England Journal of Medicine* by Stephany Seminara and colleagues. Now seventeen years later we make up the balance of what we currently know about the role of the kisspeptin and its related neurokinin B in the physiology and pathophysiology of reproduction in relation to lifetime stages such as the perinatal condition, puberty, during adult fertile life and perimenopause with focus on neuroendocrine mechanisms in the hypothalamic pituitary region. This concerns its role in episodic secretion of GnRH, the generation of the mid-cycle LH surge and the occurrence of the hot flash. With fundamental preclinical work in parallel, generated clinical knowledge today has mainly evolved from genetic studies and key pharmacological studies with kisspeptin and neurokinin B aligned analogues. Results of these studies will be reviewed and discussed in the light of promises and potential standards.

#### THE MICROBIOME AND ART

**Joop S.E. Laven, M.D., Ph.D.**

*Div. Reproductive Endocrinology & Infertility, Erasmus University Medical Center, Rotterdam, The Netherlands*

The existence of an extensive microbiome in and on the human body has increasingly dominated the scientific literature during the last decade. A shift from culture-dependent to culture-independent identification of microbes

has occurred since the emergence of next-generation sequencing (NGS) techniques, whole genome shotgun and metagenomic sequencing. These sequencing analyses have revealed the presence of a rich diversity of microbes in most exposed surfaces of the human body, such as throughout the reproductive tract. The results of microbiota analyses are influenced by the technical specifications of the applied methods of analyses. Therefore, it is difficult to correctly compare and interpret the results of different studies of the same anatomical niche. Although some microbiota are associated with reproductive success and a good pregnancy outcome, it is still unknown whether a causal link exists. For the field of reproductive medicine, determination of what is a favorable reproductive tract microbiome will provide insight into the mechanisms of both unsuccessful and successful human reproduction. To increase pregnancy chances with live birth and to reduce reproduction-related health costs, future research should focus whether on postponing treatment or conception in case of the presence of unfavorable microbiota and on the development of therapeutic interventions, such as microbial therapeutics and lifestyle adaptations.

#### NEW ASPECTS OF THE POLYCYSTIC OVARY SYNDROME (PCOS)

**Joop S.E. Laven, M.D., Ph.D.**

*Div. Reproductive Endocrinology & Infertility  
Erasmus University Medical Center, Rotterdam, The Netherlands*

Polycystic ovary syndrome (PCOS) is a diagnosis of exclusion, based primarily on the presence of hyperandrogenism, ovulatory dysfunction and PCOM. Obesity is much more common amongst women with PCOS compared to the general public. Metabolic dysfunction characterized by insulin resistance, dyslipidaemia resulting in the metabolic syndrome are frequently encountered in women with PCOS. Recent genetic studies indicate that there might be two genetically different PCOS traits being a reproductive and a metabolic phenotype. Moreover, Genome Wide Association Studies (GWAS) have identified genetic variants who are all in some ways involved ovarian function and folliculogenesis. The first Phenome Wide Association study (PheWAS) trying to associate the genetic variants with different phenotypes of PCOS in order to examine causal links between the SNP's and PCOS characteristics identified a high level of shared biology between PCOS and a range of metabolic and endocrine outcomes. Recently the association of depression, anxiety and increased levels of stress have gained increasingly attention. It seems that the way women with PCOS perceive their own bodily image impacts on these psychosocial issues. It also seems to affect sexual function in women with PCOS since they have decreased levels of satisfaction as far as sexuality is concerned. Women with PCOS are not infertile. Recent data indicate that fecundity in women with PCOS is similar to that in women without PCOS. Moreover, their reproductive life span seems to be extending into the early forties. Finally, due to an enrichment in genetic factors involved in DNA repair and maintenance they also have lower risks for aneuploidy during their fifth decade of life.

#### DELAYED FERTILITY AND LATER MENOPAUSE IN PCOS

**Joop S.E. Laven, M.D., Ph.D.**

*Div. Reproductive Endocrinology & Infertility, Erasmus University Medical Center, Rotterdam, The Netherlands*

Polycystic ovary syndrome (PCOS) is a diagnosis of exclusion, based primarily on the presence of hyperandrogenism, ovulatory dysfunction and PCOM. Metabolic dysfunction characterized by insulin resistance and

compensatory hyperinsulinaemia is evident in the vast majority of affected individuals. PCOS increases the risk for type 2 diabetes mellitus, gestational diabetes and pregnancy-related hypertensive complications. Women with PCOS might be at risk for cerebrovascular and cardiovascular events. Finally, it seems that they have an increased risk for endometrial cancer. The phenotype is not constant neither between women or within the same woman. Irregular menstrual cycles become more regular the older the PCOS women gets. Simultaneously, androgen levels decrease along with an increase in the number of ovulatory cycles. Hence women with PCOS seem to regain their fertile status later on in life compared to healthy controls. Indeed, it has been shown that they are actually not infertile or less fertile contradictory to what is generally perceived since they do conceive a similar number of children compared to non-PCOS women. Previously it was thought that this might be caused by elevated anti-Müllerian hormone (AMH) levels more profoundly inhibiting the recruitment of follicles out of the primordial follicle pool. However, recent genetic data indicate that there is a genetic basis for this because women with PCOS seem to have a selective enrichment of menopause postponing genes. These genetic variants are involved in de DNA repair and maintenance and enabling women with PCOS to handle accumulated DNA damage much more effectively compared to non PCOS individuals. This inevitably results in a longer reproductive lifespan and later menopause due to better oocyte quality compared to women without PCOS.

#### FERTILITY ENHANCEMENT USING OIL- AND WATER-BASED CONTRAST MEDIA WITH ULTRASOUND GUIDANCE

Emmeline Lee, Australia

Hystero-salpingo contrast sonography (HyCoSy) and fluoroscopic hysterosalpingography (HSG) are diagnostic tests used to assess fallopian tube patency in infertile women. Evidence shows improved pregnancy rates when oil soluble contrast (OSCM) is used rather than water soluble contrast (WSCM) during HSG<sup>1</sup>. Lipiodol is a common iodine based OSCM<sup>2</sup>. As it is well visualized on fluoroscopy, it has historically been administered under fluoroscopic guidance. In recent years, there has been increasing interest in performing Lipiodol Flushing under ultrasound guidance. Ultrasound has the added advantage of providing soft tissue evaluation prior to the procedure. This allows for the detection of contraindications (such as hydrosalpinx) and other pathologies which would contribute towards subfertility (such as endometrial polyps). In addition, there is no radiation exposure to the patient with a HyCoSy (as opposed to a HSG). Hence there is growing demand for HyCoSy using Lipiodol. Pregnancy rates following Lipiodol administration using ultrasound guidance have been similar to those performed under fluoroscopic guidance<sup>3</sup>. There also seems to be very few side effects of Lipiodol administered under ultrasound guidance.<sup>4</sup> Visibility of Lipiodol under ultrasound guidance has been questioned, and this is being increasingly studied<sup>5</sup>. Using Lipiodol safely is important, and there has been some concern regarding its use under ultrasound guidance. Many groups (including our own) are using water-based contrast media first to check for tubal patency, before the administration of Lipiodol. This allows for the detection of Intravasation, which is easily seen under ultrasound guidance with water-based contrast media. If there is intravasation with water-based contrast media, Lipiodol is then not administered. In recent years, there has been increasing concern that iodine can be retained in the body following administration of Lipiodol<sup>6</sup>. It is well known that subclinical

hypothyroidism may occur following Lipiodol HSG's. Our group has been monitoring thyroid function in the months following this, and reassuringly, there is less than 10% subclinical hypothyroidism in the patients in our most recent study. Thus, Lipiodol administration under ultrasound guidance appears to be effective in increasing pregnancy rates, and is a safe procedure.

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#### TECHNOLOGY VERSUS BIOLOGY, HOW BIOLOGY PRESENTS A LIMITATION TO PGT-A

Rajiv McCoy, USA

Whole chromosome gains and losses or “aneuploidies” are the primary cause of pregnancy loss and in vitro fertilization (IVF) failure. At the molecular level, aneuploidy exerts proteotoxic and energy stress on cells, with deleterious consequences for cellular and/or organismal fitness. Aneuploidies commonly arise during maternal meiosis, which arrests at the dictyate stage until ovulation, several decades later. Mechanisms such as premature separation of sister chromatids and reverse segregation increase in frequency with maternal age, especially around the mid-thirties. Paternal meiotic errors arising during spermatogenesis are comparatively rare and seemingly age-independent, as supported by recent large-scale sequencing studies. Intriguingly, aneuploidies arising during the initial postzygotic mitotic divisions also appear to be common in humans. Recent work demonstrates that such errors may arise by abnormal (e.g. multipolar) mitotic divisions, and/or abnormal assembly of the dual mitotic spindle that independently forms around the two parental genomes of the zygote. Such mitotic errors generate chromosomal mosaicism, with multiple karyotypically distinct cell lineages within a single embryo. Severe forms of mosaic aneuploidy disproportionately contribute to embryonic arrest prior to blastocyst formation, but mosaic aneuploidy may also arise and/or persist later in development if rescued by a sufficient number of normal euploid cells. Preimplantation genetic testing for aneuploidy (PGT-A) has been devised as a method to improve IVF success by ranking embryos for transfer based on the genomic statuses of embryo biopsies. Traditionally, all embryos that produce abnormal PGT-A results have been deprioritized for IVF transfer based. Initial iterations of PGT-A based on single-blastomere biopsies of cleavage-stage embryos were hampered by high rates of mosaicism, in part leading to the transition toward blastocyst-stage PGT-A where mosaicism is less prevalent. Meanwhile, technical platforms have improved and the increased sensitivity and resolution of low-coverage whole-genome sequencing-based PGT-A have placed renewed focus on chromosomal mosaicism as a

potential confounding factor. In addition to the technical challenges surrounding its detection, the clinical consequences of chromosomal mosaicism remain poorly understood. Here I will review recent work describing the mechanistic origins of aneuploidy in human preimplantation embryos and the implications for PGT-A. Integrating evidence from PGT-A, time-lapse, and single-cell sequencing, I will synthesize recent insights into the origins of both meiotic and mitotic aneuploidy and their evolution throughout development. This review will cover the current state of knowledge about the genetic and environmental factors that modulate aneuploidy risk and whether such knowledge can guide individualized risk assessment and fertility planning. I will focus on the ways that computational and statistical methods can be leveraged for biological understanding, improved clinical tests, and evaluation of uncertainty. This includes addressing the relevant but elusive question of whether rates of aneuploidy vary across cell types of the differentiating embryo—a question with key biological and clinical implications that has achieved substantial recent attention based on work in both humans and model organisms. Such mechanistic knowledge offers new opportunities for classifying embryos based on PGT-A and other forms of data, and I will discuss my lab's recent work leveraging algorithms inspired by population genetics toward this end.

## BRCA2 AND FANCM MUTANTS IN PRIMARY OVARIAN INSUFFICIENCY WITHOUT CANCER OR FANCONI ANEMIA TRAIT

Abdelkader Heddar, MD<sup>1</sup>, and Micheline Misrahi, MD, PhD<sup>1,\*</sup>

<sup>1</sup>Faculté de Médecine, Université -Paris-Saclay, Hôpital Bicêtre, 94275, Le Kremlin Bicêtre, France

Primary Ovarian insufficiency (POI) affects 1% of women under 40 years and is a public health problem. The genetic causes of POI are highly heterogeneous with isolated or syndromic forms. Recently, mutations in genes involved in DNA repair have been shown to cause POI but their consequences in health outcome apart from infertility is unknown.

We have studied two consanguineous families, one with two sisters displaying POI and incipient POI, and the second with a POI patient.

Using exome sequencing, we surprisingly uncovered a homozygous pathogenic variant of FANCM or BRCA2 genes involved in the Fanconi anemia pathway in our patients causing POI but without cancer or FA in all their families.

BRCA2, is a gene with a critical role in DNA repair and homologous recombination in somatic cells. Patients with BRCA2 biallelic mutations develop Fanconi Anemia, a severe life-threatening condition characterized by pancytopenia and multiple malformations and malignancies, while women with monoallelic alteration are at high risk to develop breast or ovarian cancer (up to 60%).

We show in our studies that both variants are hypomorphic, explaining very probably the early impairment in meiosis yielding POI, but the absence of somatic pathologies as tumor/cancers that the residual activity of the proteins could explain.

The homozygous missense p.R2842C BRCA2 variant only mildly altered the function of the protein using several in vitro functional assays in primary and lymphoblastoid immortalized cells. We show that the patient's cells showed intermediate levels of chromosomal breaks, cell proliferation and radiation-induced RAD51 foci formation compared to controls and FA cells. The mutant BRCA2 only partially (~30%) complemented

homologous recombination efficiency compared to wild type BRCA2.

Our findings extend the phenotype of BRCA2 bi-allelic alterations to fully-isolated POI. This study has a major impact on the management of patients with POI and the genetic counselling that should now be addressed while keeping in mind a possible defect in a major DNA repair gene such as BRCA2.

As DNA repair genes is leading cause of POI, this means that all such patients should have a long-term follow-up in a multidisciplinary teams to detect possible co-morbidities in the future. Precautions must be taken such as the absence of physical or chemical aggressions because weak defects of DNA repair can be demonstrated in their cells.

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## UNDERSTANDING THE GENETICS OF POI IS IMPORTANT IN CLINICAL PRACTICE FOR THE MANAGEMENT OF AFFECTED WOMEN AND THEIR FAMILIES

Abdelkader Heddar, MD<sup>1</sup>, and Micheline Misrahi, MD, PhD<sup>1,\*</sup>

<sup>1</sup>Faculté de Médecine, Université -Paris-Saclay, Hôpital Bicêtre, 94275, Le Kremlin Bicêtre, France.

Premature ovarian failure (POI) is a syndrome observed in 1% of women under 40 years old most often resulting in permanent infertility, leading to egg donation or adoption. However, there are fluctuating POI with reversible ovarian function. An unrecognized follicular pool may therefore persist. The assessment of this residual follicular pool is an essential element of the prognosis and should lead to appropriate genetic and therapeutic counseling.

However, there is no strategy of diagnosis or management established to date.

Three main mechanisms can be identified: 1) impaired establishment of the follicular pool, 2) increased atresia, 3) or alteration in follicular growth. In the latter case, identifying the cause could help establish a prognosis for fertility.

We have developed a Next Generation Sequencing-NGS panel comprising all the genes currently known to be responsible for POI (80 genes). With this panel we can find the cause of POI in ~30% of patients. Our NGS strategy optimizes the molecular screening of POI and confirms the great genetic heterogeneity of this syndrome.

The genetic study is essential to 1) identify the cause of POI 2) to allow personalized management and appropriate genetic counseling 3) to detect and treat associated comorbidities or to preserve residual fertility depending on the genetic defect observed.

- In 1/3 of cases, meiosis or DNA repair genes are involved. Complete study of patients with search for associated comorbidities allows suitable genetic and therapeutic counseling in the family. If there is a parental project, oocyte donation or adoption will be proposed.

The new link between the genes responsible for POI and tumor / cancer genes makes the genetic diagnosis of any POI necessary. It markedly changes the management of these patients and their families. Long-term follow-up within a multidisciplinary team is necessary.

- In 1/3 of cases an abnormality of genes involved in follicular growth is found. In these cases a reversible POI can be predicted depending on the cause, and the persistence of an ovarian reserve should lead to fertility preservation. Indeed, innovative follicular activation techniques are currently being developed in vitro.

- Finally, in 20% of cases, patients with syndromic POI are initially thought to be isolated POI. This requires a complete familial study of possibly associated comorbidities. The prognosis for fertility is sometimes good, as in the case of an observed mutation in the GALT gene observed in one of our patients.

• It is therefore important to propose a diagnosis strategy and recommendations for the genetic study of POI that do not currently exist.

- We must estimate the proportion of patients with a genetic cause suggesting the persistence of an ovarian reserve. Very recently, in vitro activation of small follicles or of "dormant follicles" was obtained for POI with recovery of fertility in some patients.
  - The search for associated comorbidities also depends on the etiology.
  - The genetics of POI has been recognized as a priority in France and is one of the first pathologies for which a Whole Genome Sequencing is proposed when the NGS panel of 80 genes is negative. This is part of the new "Plan France Médecine Génomique 2025". Complex abnormalities of known genes or of new genes can thus be highlighted, further increasing the proportion of genetic diagnosis in the future.
- POI is a syndrome with multiple causes and appropriate management with personalized medicine must be developed.

## NATURAL HISTORY OF HPV AMONG FEMALES: IMPLICATIONS FOR CONTROL

**Anna Barbara Moscicki**

*Department of Pediatrics, University of California, Los Angeles, USA*

Although epidemiologic studies have given us insight into the natural history, many pieces remain missing including transmission dynamics and the final steps required for the transition from CIN 3 to invasive cancer. Current studies show young women appear the most vulnerable to acquiring HPV and that the majority of casual HPV (those that lead to cancer) occur by age 25 years. But not all countries show a peak in young women and 90% of those infections in young women "regress". It has also become clear that "detection" does not necessarily equate with "infection" and may reflect partner contamination. Innate immune responses to HPV are likely critical to clearance of initial infections and adaptive immune response for clearance after persistence. The higher rate of transmission from females to males than vice versa suggest women are more likely to develop strong T-cell memory. The longer the persistence, the more likely the infection will not clear, and precancerous CIN 3 becomes almost inevitable. Recent data suggest that the vaginal microbiome plays a

critical role in the natural history and that Lactobacillus-dominant microbiomes assist in viral control. The final stages of cancer development are likely multi-faceted as in many cancers but include HPV's ability to cause cell cycle dysregulation and/or viral integration with loss of tumor suppressor gene function or increased expression of oncogenes. The low positive predictive value of an HPV positive test underscores the complexity of the natural history of HPV and the importance of targeting pre-sexually active youth for vaccination.

## IMPACT OF COVID-19 ON CLINICAL MANAGEMENT OF WOMEN WITH GYNECOLOGICAL CANCER

**Sara Nasser, Germany**

The novel coronavirus disease (COVID-19) is a global public health emergency that has impacted medical professionals, infrastructures and the care of patients with gynecological malignancies. The pandemic has also caused disruption to research and clinical trials across Europe and worldwide. We conducted a collaborative Survey within Europe and the panarabian region to evaluate the impact of the COVID-19 Pandemic on the management of patients with gynecological malignancies from the multidisciplinary physicians' perspective, with particular focus on clinical infrastructures, trial participation and maintenance therapy. The survey is designed to capture the dynamic changes observed with the development of the pandemic in order to build robust emergency algorithms tailored to gynecological oncology patients in the future.

## NEW SERMs/TSEC: CAN THEY BE AN HRT SUSTITUTIVE

**Santiago Palacios**

*Director of the Instituto Palacios de Salud y Medicina de la Mujer, Madrid, Spain*

SERMs are compounds with a molecular structure different from that of steroids. They share their selective binding to estrogen receptors (ER) with steroids and produce an estrogen agonist or antagonist effect depending on the target cell and hormonal environment. They have been developed with the aim of producing specific positive estrogenic effects on some target tissues, but with negative or neutral estrogenic effects on other tissues (1). To understand the mechanism of action of SERMs, we must remember how estrogen works. After the binding of the hormone to the receptor, a hormone-receptor complex is formed, which in turn binds to another complex of the same characteristics to form homodimers, which acquire a unique spatial configuration and bind to DNA with high affinity and to different cofactors and stimulate or inhibit gene transcription by means of the AF-1 and AF-222 regions. The DNA region to which the activation domains or activation factors of the AF-1 and AF-2 transcription are attached is called the estrogen response element (ERE), which is a specific area and which, thanks to the spatial structure created by the hormone-receptor complex and its attachment to this area of DNA, causes a series of specific cofactors to bind together and activate or repress a series of genes (2). To explain why the response induced by SERMs, after their binding to the receptor, may be similar or different from that induced by estrogens themselves, the spatial configuration of the SERM-receptor complex must be understood. Thus, after its binding to the receptor, the SERM creates an anomalous configuration of the hormone-receptor complex that causes it to be located in a different area of the DNA from the ERE and to bind to another type of co-factor,

which entails another type of message and genetic expression. This makes each SERM unique (3-4).

#### NEW SERMs/TSEC

**Ospemifene:** Ospemifene belongs to the family of triphenylethylenes. It is a biologically active metabolite of toremifene (desamino-hydroxy-toremifene) that demonstrated prevention of bone loss and reduced cholesterol levels in castrated rats without weight gain in the uterus (5). In addition, in in vitro studies it acts as a potent estrogen antagonist in ER-positive breast cancer cell lines (6). Ospemifene greatly reduces the incidence of breast carcinomas in comparison to control mice and was similar to tamoxifen in dimethylbenzanthracene (DMBA)-induced breast tumors (7). Ospemifene proved more estrogenic than raloxifene, as shown by changes in serum levels of follicle-stimulating hormone and sex hormone-binding globulin. Neither ospemifene nor raloxifene stimulated the endometrium, but in contrast to raloxifene, ospemifene had a clear estrogenic effect on the vagina (8). For this reason, a comprehensive clinical program was conducted on its effect on vulvovaginal atrophy. We can conclude that it is the first non-hormonal oral alternative for vulvovaginal atrophy. It is a selective estrogen receptor modulator (SERM) that selectively exerts agonistic effects on vaginal tissue. 60 mg ospemifene has been shown to reduce symptoms of dyspareunia and vaginal dryness significantly compared to placebo and to be safe at 52 weeks (8,9)

**Bazedoxifene:** Bazedoxifene is one of the newest SERMs recommended for the prevention and treatment of postmenopausal osteoporosis. Thus, in a meta-analysis of 4 randomized and placebo-controlled trials, it is concluded that the use of bazedoxifene reduces the incidence of vertebral fractures and increases bone mineral density at 3 and 7 years. Furthermore, serious adverse events such as myocardial infarction, stroke, venous thromboembolic events and breast cancer do not increase during this period of use (10, 11)

**TSEC:** A new approach to hormone therapy is to combine an estrogen with a SERM in order to achieve all the positive effects of estrogens and even increase them and avoid their negative effects by using a SERM, and this combination is called the Tissue Selective Estrogen Complex (TSEC). The purpose is to decrease hot flushes, prevent and treat vulvovaginal atrophy, and prevent bone loss, without stimulating the breast or endometrium. Bazedoxifene in combination with conjugated estrogens in doses of 0.45 or 0.625 mg significantly reduces vasomotor symptoms (12), improves vaginal symptoms (12), and increases bone mineral density in the lumbar spine and hip (12). It is clear that this is a promising treatment for both vasomotor symptoms and the prevention of osteoporosis (13). **Conclusions:** SERMs are non hormonal alternatives to treat different symptoms and or risks of postmenopausal women. Another interesting concept would be TSEC, a combination of bazedoxifene with conjugated estrogens as a possible alternative to classical hormonal treatment and which opens up the possibility of different combinations. Meanwhile, the rapid developments in the molecular biology of the ER activation cascade, together with advances in genomics and chemistry and proteomics, makes us optimistic about the future of different estrogen modulators in the medium term.

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#### IS THERE A NEED FOR A PREMATURE OVARIAN INSUFFICIENCY (POI) NETWORK / DATABASE? Nick Panay, UK

**Context:** Premature ovarian insufficiency (POI) remains poorly understood and under researched. Guidelines from ESHRE, IMS, EMAS and NICE UK have been developed using data largely from observational and short term RCTs. The challenges with relatively rare diseases such as POI are that they:

- limit the experience of any one centre
- are incompletely characterized, with few data on long term outcomes
- induce fragmented research and patient care

The POI registry <https://poiregistry.net> was developed at Imperial College London (ICL), UK using a British Research Council grant to collect national/ international data in an effort to facilitate collaborative research and improve our understanding of this important disease. **Objective:** Retrospective and prospective network analysis of women with POI. **Methods:** Data collected on women diagnosed with POI < 40 years were entered onto an online registry using the semantic web. The data were extracted and analysed at ICL by patient ages, etiology, ethnicity, time to diagnosis, symptom profile and bone mineral density (BMD). **Results:** More than 60 centres have registered to enter data globally. Many centres are in the UK but also include investigators in Australia, Canada, Chile, Italy, Russia, Spain and South Africa. Retrospective and prospective data for more than 800

women with POI have been entered thus far. A further 400 patients have been entered into a Chinese translation of the registry at Beijing ObGyn Hospital, Capital Medical University and will be merged. Data include demographics, diagnosis, presentation, management and outcomes e.g. delay to diagnosis was found to be associated with progressively lower bone mineral density. Collaborative work is now planned to facilitate biobanking for genetic and biomarker analyses.

**Conclusions:** The POI registry has proved successful given the number of centres and patients registered thus far. By encouraging more healthcare professionals to engage with data collection, we aim to optimize the quality and quantity of data. Long term successful collaboration with our international colleagues will improve the diagnosis and treatment of most aspects of POI.

## PHARMACODYNAMICS: WHAT TO KNOW?

Paul Piette, PharmD

Senior Research Fellow, Besins Healthcare Global

This review explains why micronised P4 and synthetic progestins cannot be considered as a single pharmacological class, and looks at the impact that their different chemical structures, structure-function relationships, metabolism, pharmacokinetic and pharmacodynamic parameters have on their efficacy and safety profiles, particularly when used during early and late pregnancy.

The route of administration is crucial in determining the optimal pharmacodynamic profile of P4, in terms of both the desired and reliable clinical effects, particularly during pregnancy. Compared with oral ingestion, vaginal administration of P4 results in only a small increase in the metabolite allopregnanolone and no change in 5 $\beta$ -pregnanolone levels, because normal vaginal bacteria are devoid of 5 $\alpha$ - and 5 $\beta$ -reductases. This explains why the activity of P4 on the CNS is affected by the route of administration. The vaginal route induces a lower C<sub>max</sub> and higher P4 blood levels at steady state compared to oral administration and similar t<sub>1/2</sub> values with more constant blood levels during the nycthemeral period. As a result, P4 vaginal administration is highly effective in inducing the secretory transformation of the endometrium and in preventing premature shortening of the cervix. It is the preferred therapy for the maintenance of pregnancy, with only minor changes in the plasma levels of the "psychotropic" metabolites.

Comparisons of i.m. and vaginal P4 dosing for luteal phase support (LPS) in infertility treatments has led to both controversial results and considerable debate over the best routes of administration, particularly in the USA. Studies have shown that despite discrepancies detected between serum levels and histological endometrial features after vaginal P4 application, adequate secretory endometrial transformation can be reached, with minimal undesirable systemic effects.

An updated worldwide web-based survey has assessed the real-life clinical practices regarding LPS in assisted reproduction: based on data obtained from 408 centres in 82 countries, representing 284,600 IVF cycles/year, it has been shown that most practitioners used a vaginal P4 product in more than 90% of the cycles (77% as a single agent and 17% in combination with i.m. progesterone).

Two important metabolites of P4, allopregnanolone (3 $\alpha$ ,5 $\alpha$ -tetrahydroP4) and 3 $\alpha$ ,5 $\alpha$  tetrahydrodeoxycorticosterone, are natural positive modulators of the neuronal GABA<sub>A</sub> receptor. These provide a clear pathway that explains the rapid psychopharmacological actions, including anxiolytic, antidepressant, anaesthetic, anticonvulsant and analgesic effects seen with different dosages and routes of administration. During pregnancy not only the maternal brain

but also the placenta may contribute directly and indirectly to an increase in allopregnanolone production and activity in the foetal brain, modulating neuroendocrine responses to stress. Luteal P4 and oestradiol are an essential requirement for preparing the uterus for implantation. When no other apparent causes of infertility are detected, assisted reproduction techniques (ARTs) can be avoided and replaced by individualised P4 supplementation during the early luteal phase in a natural cycle. P4 is crucial for the establishment of pregnancy because of its roles in activating several P4-regulated genes in the pregnant uterus and in the development of endometrial receptivity to permit implantation. Early in pregnancy P4 is produced by the corpus luteum and the rise in P4 production is fundamental for the maintenance of pregnancy until the placenta takes over this function at 7-9 weeks of gestation. At term, the placenta produces about 250 mg P4 per day. Placental P4 maintains many of the distinct properties of the pregnant uterus and cervix, including immunological and anti-inflammatory functions. P4 and some progestins can affect the serum concentrations of other hormones, particularly oestrogen. Oestrogenic effects are modified by P4 or progestins, either by reducing the availability or stability of the hormone receptor complex or by turning off specific hormone-responsive genes by direct interaction with the P4 receptor in the nucleus. Oestrogen priming is necessary to increase progesterone effects by up regulating the number of P4 receptors and/or increasing P4 production, causing a negative feedback mechanism that inhibits oestrogen receptors. This negative feedback system protects the pregnancy by ensuring that the correct amount of oestrogen and P4 are present to maintain the lining of the uterus, prevent contractions of the smooth muscle, trigger the development of the foetal organs, etc.

Ovarian hyperstimulation for IVF shortens the luteal phase resulting in advanced luteolysis. In the absence of LPS in controlled ovarian stimulation (COS) cycles, maturation of the endometrium is unsatisfactory, and the histological dating never corresponds to the expected cycle day. After administration of exogenous micronised P4, the endometrial morphology is indistinguishable from that of a natural cycle. A study in women with ovarian failure (primary or secondary) preparing for embryo transfer (ET) following oocyte donation has shown that after i.m. administration of P4, the endometrial morphology may be less homogeneous than following vaginal administration, with 43.5% of specimens showing delayed maturation and 9% of specimens showing glandular/stromal asynchrony. The net consequences of premature P4 elevation on IVF-ET outcome might result from a balance between two antagonistic parameters: good embryo quality is associated with a good ovarian response to COS correlated with higher P4 levels but impaired receptivity of the endometrium resulting from premature endometrial exposure to P4.

## LUTEAL PHASE SUPPORT: BALANCING EFFECTIVENESS AND SAFETY

Peter Platteau, Belgium

Luteal phase support (LPS) aims to increase progesterone levels during the luteal phase of the menstrual cycle, which is the phase following ovulation. This can be achieved by administration of progesterone, dydrogesterone, human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone agonist (GnRHa). Progesterone supplementation can be administered vaginally with a progesterone gel or in capsules of natural micronised progesterone, orally in capsules of natural micronised progesterone, by intramuscular injections of progesterone in oil or by

subcutaneous injections of progesterone. With regard to natural progesterone, oral preparations are of limited use in reproduction because they have poor bioavailability. Vaginal preparations are associated with vaginal discomfort and discharge, but they yield high serum concentrations by bypassing the first-pass effect through the liver, achieving adequate endometrial transformation and sustained circulating levels across 24 hours. Intramuscular oil-based progesterone achieves good levels of circulating progesterone, but the injections cause discomfort and pain. A novel aqueous progesterone preparation is administered subcutaneously that might result in similar progesterone levels with less pain than can be achieved with intramuscular preparations. Dydrogesterone (6-dehydro-retroprogesterone) is structurally and pharmacologically similar to natural progesterone, and it has good oral bioavailability and better tolerability than vaginal progesterone. Human chorionic gonadotropin is similar to LH in its molecular structure but has greater potency and a longer serum half-life, working as LPS by stimulating the corpus luteum to produce progesterone; it is administered by subcutaneous or intramuscular injections. HCG is not much used these days in ART due to the increased risk of Ovarian hyperstimulation (OHSS). Gonadotropin-releasing hormone agonist increases LH secretion by the pituitary, resulting in increased progesterone production by the corpus luteum; it is frequently administered by subcutaneous daily injections or by nasal spray. High oestradiol and progesterone levels due to ovarian stimulation exert direct negative feedback at the pituitary gland, reducing LH secretion and thereby impairing the ability of the corpus luteum to produce sufficient levels of progesterone to maintain pregnancy. Clinicians have to choose the LPS they want to give to their patients, balancing the pros and cons of the most effective, cheapest, patient friendly and safest drug.

## CO2 LASER APPLICATIONS IN GYNAECOLOGY

**Stefano Salvatore**

*San Raffaele Vita e Salute University, Milan, Italy*

CO2 laser is a sophisticated technology whose use in gynaecology is constantly increasing. If we exclude the vulvar conditions, CO2 laser is commonly used to treat different conditions such as stretchmarks, scars, Minor labia hypertrophy, endometriosis and ovarian endometriotic cysts (with an improvement of the ovarian residual function compared to the classical techniques), the genitourinary syndrome of menopause (including vulvovaginal atrophy symptoms and lower urinary tract symptoms). During my presentation I will cover all these aspects, focusing, in particular on GSM treatment outcome. Available evidence based will be provided looking at animal studies, histology, biochemical results, microbiology and clinical studies. These ones will be presented with historical data, systemic reviews and metaanalysis and randomized controlled trials. At the end of this excursion CO2 laser results to be a safe and effective treatment for all the above mentioned conditions. Certainly its use in the treatment of GSM continues to provide a growing evidence that hopefully will convince scientific societies to insert it in the proposed treatment algorithm for this condition.

## INDUCTION OF LABOR FOR WOMEN WITH DIABETES IN PREGNANCY? No

**Ute Schaefer-Graf MD PhD, Germany**

Pregnancies of women with diabetes are considered as high-risk pregnancies, however there is a wide range of severity of deterioration of glucose metabolism from long lasting preexisting diabetes with poor glucose control to mild

gestational diabetes managed well with minor lifestyle modification. Therefore, arguments for or against induction of labor and the timing have to differentiate for the individual risk profile of the women. In women with preexisting diabetes, most guidelines recommend induction with 38 weeks, in the presence of additional complications even earlier. Same for gestational diabetes treated with insulin, for diet treated women at term. This is based on the increased risk for intrauterine demise in women with diabetes. There is a paucity of data that show the evidence that the request of early delivery is justify in every insulin treated women with diabetes, most observational studies did not consider all maternal or fetal parameters which potential impact of the risk for IUFD. Induction and delivery at 38 weeks implicates longer hospital stay, absorbs personal capacity, neonatal problems due to immaturity and is a burden and often unpleasant birth experience for the women. An individual risk score involving preconceptional HbA1c, pregnancy course, glucose control during pregnancy, maternal complication and fetal growth pattern would allow more targeted delivery planning and delayed induction at term instead of the request

## BISPHENOL A AND REPRODUCTIVE TOXICOLOGY

**Gilbert Schönfelder**

*German Federal Institute for Risk Assessment, Berlin, Germany | Charité Universitätsmedizin Berlin, Berlin, Germany*

According to the definition of the World Health Organization, an environmental chemical is classified as an endocrine disruptor (EDC) if it alters the function(s) of the endocrine system and causes adverse health effects in an intact organism, its progeny or (sub) populations. Bisphenol A (BPA) is an industrial chemical that develops hormone-like (including estrogen-like) effects. BPA serves primarily as a starting material for the synthesis of polymeric plastics and is therefore mostly found in plastics and epoxid resins. BPA is also found in thermal paper through which it can expose humans. In fact, various scientific studies show that humans are exposed to BPA at different stages of life, including pregnant women and their children in the uterus. Various scientific studies have been conducted over the past two decades to test whether BPA is an endocrine disruptor and can have reproductive toxicological effects. The many toxicological studies led to a permanent revision of the current risk assessment of BPA, which has been the subject of controversial scientific discussions worldwide for years. Finally, in 2017 the European Chemical Agency (ECHA) listed BPA in the Candidate List of substances of very high concern (SVHCs) due to its toxic for reproduction properties. ECHA classified BPA as an EDC "which cause probable serious effects to human health which give rise to an equivalent level of concern to carcinogenic, mutagenic, toxic to reproduction (CMRs category 1A or 1B) substances". However, the European Food Safety Authority (EFSA) points out that if the provisionally established tolerable daily intake (temporary TDI) is adhered to, no adverse health effects of BPA are expected to humans. The definition of the TDI is the estimated quantity of any given substance, which can be ingested every day of a person's entire life without having any tangible effects on his or her health.

## FREEZE-ALL SERVES TO CIRCUMVENT A FAULTY ENDOMETRIUM

**Bruce S. Shapiro, USA**

Controversy continues to surround the efficacy of a freeze-all approach to IVF as opposed to fresh transfer. To accurately frame the question, three important historical findings should

be considered. First, controlled ovarian hyperstimulation (COH) accelerates endometrial development and can compromise embryo-endometrial synchrony. Second, cryopreservation can damage embryos and this damage might not be visible immediately post thaw. Third, synchrony between embryonic and endometrial development, including progesterone initiation, can be precisely controlled in cycles of frozen-thawed embryo transfer (FET). Therefore, the relevant question here is “Can superior embryo-endometrial synchrony in FET cycles compensate for embryo cryodamage and, if so, for which populations and by which methodologies?” A body of research stretching back >20 years has found endometrial histological development and progesterone receptor down-regulation were each advanced by about 2 days in COH cycles when compared to natural cycles. This advancement is exacerbated by premature progesterone elevation and is associated with decreased success rates after fresh embryo transfer. Furthermore, gene regulation is altered following COH. One author succinctly stated the endometrium is “histologically advanced, biochemically different, and genomically dysregulated” in COH cycles. Clinically, fresh day 5 blastocysts implant much more readily than day 6 counterparts in endometria exposed to COH. However, this advantage is reduced or absent in cycles where endometria were not exposed to COH, such as FET and oocyte donation cycles. This effect has been attributed to embryo-endometrial asynchrony in fresh autologous cycles. Premature progesterone has also been associated with decreased implantation and reduced pregnancy rates in fresh cycles, which is also mitigated by cryopreservation and subsequent transfer in cycles without uterine COH exposure. Annual US national registry reports have shown success rates per transfer to be superior in fresh oocyte donation cycles when compared to fresh autologous cycles in the youngest age group. This effect vanishes when corresponding FET cycles are compared, suggesting the advantage of donor cycles over autologous cycles in young patients is secondary to uterine COH exposure in the fresh autologous cycles. Two early randomized controlled trials (RCTs) were performed to compare endometrial receptivity in fresh and FET cycles. In these studies, patients were randomized to have either fresh blastocyst transfer following COH or else have all embryos frozen, followed by thaw and blastocyst transfer. While the clinical pregnancy rate was greater with thaw transfer than with fresh transfer in both studies, only the study in normal responders showed a statistically significant difference, while the study in high responders did not, although the latter study was stopped early due to safety concerns from excessive twin rate. The conclusion of the former study was that endometrial receptivity is impaired by COH in some patients. There have been three subsequent RCTs comparing overall efficacies of fresh and FET cycles using cleavage-stage transfer. Two of those studies found no significant difference while the other, a study in patients with polycystic ovarian syndrome, found the FET arm to have superior success rates. Two RCTs comparing overall efficacies of fresh and FET cycles using blastocyst transfer found thawed blastocysts were more likely to implant, while a third study found no significant difference. The variation in the results of these studies might be due to population differences or protocol differences involving embryo stage at cryopreservation, embryo stage at transfer, embryo selection, cryopreservation, and luteal support. Successful FET cycles require adequate endometrial preparation, precise transfer timing, and ample luteal support, and post-thaw viability assessment that includes resumed development. In addition, embryo selection for transfer should be similar and optimal in each arm of such RCTs. There have also been many studies, including several registry studies and meta-analyses, comparing perinatal risks in fresh

and FET cycles. These studies have generally found fewer perinatal risks after FET, many of which are defined by birthweight. Comparisons of singleton birthweights have usually found 100-200g reduction in birthweight in fresh transfers following uterine COH exposure when compared to FET or natural cycles. This birthweight decrease results in increased risk of small-for-gestational-age but also reduced risk of large-for-gestational-age infants. Some early researchers feared birthweight differences might be due to some embryonic effect from cryopreservation, such as epigenetic effects. However, studies that also included births from natural conceptions consistently found FET birthweights to be similar to those from natural conceptions, in contrast with birthweights following fresh transfers that were consistently found to be less than those following natural conceptions. Furthermore, studies comparing birthweight following fresh and FET in oocyte donation cycles, where there typically is no uterine COH exposure in either group, found no significant difference in birthweight, suggesting no direct effect of cryopreservation on birthweight. Therefore, the observed birthweight effects in autologous cycles are probably due to endometrial effects of uterine COH exposure reducing birthweight when compared to FET and natural conceptions. Maternal risk comparisons have generally found FET to have reduced risk of ectopic pregnancy and ovarian hyperstimulation syndrome (OHSS), but increased risk of pregnancy-induced hypertension (PIH). Interestingly, increased risk of PIH has also been noted in donor cycles, whether using fresh transfer or FET, and in gestational carriers. This suggests an unknown uterine effect, perhaps from the artificial endometrial preparation common in these cycles. Thus far, every study comparing fresh versus thawed embryo transfer has used identical COH protocols in each study arm. This approach is appropriate for assessing the impact of COH on endometrial receptivity but has limitations when comparing overall method efficacies. COH protocols for fresh transfer have been largely optimized over four decades, while COH protocols for freeze-all cycles have yet to be optimized. There are COH options exclusive to the freeze-all cycle. These include random-start COH to potentially reduce time-to-pregnancy, progestogen for hypothalamic down-regulation to reduce cost, prolonged stimulation regardless of progesterone elevation to obtain more oocytes and embryos to increase success rates, and use of agonist “trigger” to reduce OHSS risk. It is currently unclear whether risks are reduced if natural cycles are used instead of artificial cycle preparation for FET, donor, and GC cycles. Optimization and standardization of luteal phase support in freeze-all protocols may further improve outcomes and reduce risks. Until these protocols are optimized and standardized, conclusions from randomized trials and meta-analyses comparing efficacies may be premature. Today, it is possible to routinely achieve 60% live birth rate with single blastocyst transfers in FET, avoiding the risks associated with the transfer of multiple embryos.

#### DOES PRESENCE OF ADENOMYOSIS AFFECT REPRODUCTIVE OUTCOME IN IVF CYCLES? A RETROSPECTIVE ANALYSIS OF 973 PATIENTS

Sunita Sharma, Shikha Bathwal, Nupur Agarwal, Ratna Chattopadhyay, Indranil Saha, Baidyanath Chakravarty, *India*

**Research question:** Reports on the effect of adenomyosis on assisted reproductive technology (ART) outcomes are conflicting. Does presence of adenomyosis affect reproductive outcome in IVF cycles in women pretreated with gonadotrophin releasing hormone (GnRH) agonist? **Design:** In this retrospective cohort study, 973 women were divided into four groups: only endometriosis ( $n = 355$ ); endometriosis

and adenomyosis ( $n = 88$ ); adenomyosis alone ( $n = 64$ ); and tubal factor infertility as controls ( $n = 466$ ). The pregnancy outcome parameters (clinical pregnancy, miscarriage rate, live birth rate) were compared between these groups. **Results:** The clinical pregnancy rate was 36.62% in women with endometriosis alone, 22.72% in women with endometriosis and adenomyosis, 23.44% in women who only had adenomyosis and 34.55% in controls. Miscarriage rates were as follows: 14.62%, 35%, 40% and 13.04%, respectively. Live birth rates were 27.47% in controls; 26.48% in women with only endometriosis; 11.36% in women with endometriosis and adenomyosis; and 12.5% in women with only adenomyosis. Live birth was observed to be less in adenomyosis groups compared with controls and women with only endometriosis. No significant difference was observed in clinical pregnancy, miscarriage or live birth rate between controls and women with only endometriosis. Live birth rate was significantly different between controls and women with adenomyosis only ( $P = 0.01$ ) and women with endometriosis and adenomyosis ( $P = 0.002$ ). **Conclusion:** Presence of adenomyosis seems to have adverse effects on IVF outcomes in clinical pregnancy rate, live birth rate and miscarriage rate. Screening for adenomyosis might be considered before ART so that the couple has better awareness of the prognosis.

#### DO MEN WITH NORMAL TESTOSTERONE-OESTRADIOL RATIOS BENEFIT FROM LETROZOLE FOR THE TREATMENT OF MALE INFERTILITY?

**Liu Shuling**, Matthew Lau Sie Kuei, Seyed Ehsan Saffari, Zheng Jiayun, Tan Tse Yeun, Jessie Phoon Wai Leng, Veronique Viardot- Foucault, Sadhana Nadarajah, Jerry Kok Yen Chan, Tan Heng Hao, *Singapore*

**Research question:** Previous studies of aromatase inhibitors on male infertility have focused on men with low testosterone–oestradiol ratio of less than 10. Can aromatase inhibitors improve spermatogenesis in men with idiopathic male infertility with normal testosterone–oestradiol ratio? **Design:** Prospective study of men with idiopathic severe oligozoospermia (sperm concentration  $<5$  million/ml) carried out between February 2015 and March 2017. The objective was to assess if semen-analysis parameters improved after treatment with letrozole. Secondary objectives were to monitor the safety of letrozole in men, and to measure the alterations in serum FSH, LH, oestradiol and testosterone levels. **Results:** Fifteen men with normal testosterone–oestradiol ratio ( $>10$ ) were treated with letrozole 2.5 mg daily for 4 months. This produced a 5.5-fold increase in sperm concentration ( $P = 0.0068$ ). All men had increased total serum testosterone and suppressed oestradiol levels after treatment, thus raising the overall testosterone–oestradiol ratio ( $P < 0.0001$ ). Adverse effects from letrozole were relatively minor and included loss of libido (54%), headaches (25%), fatigue (21%), weakness (13%), loss of hair (8%) and dry mouth (8%). **Conclusions:** Letrozole improves sperm concentration and increases testosterone–oestradiol ratio for men with oligozoospermia who have normal testosterone–oestradiol ratio; its role in the treatment of male infertility may be extended to this group of patients. In addition, it is a relatively well-tolerated drug with no serious adverse effects.

#### FERTILITY PRESERVATION FOR WOMEN WITH ENDOMETRIOSIS: NO

**Edgardo Somigliana**, *Italy*

Fertility preservation is an emerging and fascinating area of medicine. Outstanding achievements have been reached in

just two decades. Women with cancer once frequently condemned to future childlessness can now face their reproductive future with less apprehension. In fact, fertility preservation before cancer treatments has become part of routine clinical practice in Western societies. Nonetheless, as for all new technologies, there is the consistent risk of indication creep. That is, once a new technology has been accepted and adopted for use in one clinical area or patient group, its use can spread to other patient groups, without formal consideration of cost-effectiveness. Fertility preservation for endometriosis is an excellent example. Endometriosis can affect fertility and surgery can injure ovarian reserve. On these bases, one is tempted to claim fertility preservation for all affected women at the time of first diagnosis. However, endometriosis is a common disease and a blind plea for fertility preservation may have devastating consequences. Prior to recommend this approach, we do need robust without robust clinical and economical evidence. However, up to now, this type of evidence for endometriosis is lacking. Some case series have been published but they are poorly informative. The crucial point here is not whether or not fertility preservation is feasible in women with endometriosis (for sure it is feasible). The main issue is measuring the additional benefit that fertility preservation could provide and weight this advantage with the general costs for the community. Noteworthy, the rate of women thawing their frozen oocytes reported in some of the available case series do not reflect the real benefit. One should consider that some (many) of the women who stored their egg may have also conceived using fresh IVF. In other words, these women should be subtracted from the nominator. In addition, one may consider that oocytes retrieval may be more risky in women with endometriosis, in particular in women with ovarian endometriomas or severe adhesions displacing the ovaries behind the uterus. Overall, claiming for fertility preservation in women with endometriosis is premature and unwise. Endometriosis as an indication to fertility preservation is experimental. At present, this option may be considered only in referral centers and in highly selected cases but should not become routine practice.

#### GUT BRAIN: ITS ROLE IN WOMEN'S HEALTH

**Vincenzo Stanghellini**

*IRCCS S. Orsola, University of Bologna, Italy*

The Central Nervous System (CNS, or big brain) is not the only brain of the human body, since the Enteric Nervous System (ENS, or little brain) consists of a number of neurons that is equal to that of the spinal cord and acts as an independent brain, capable of organizing the complexity required by digestive functions. Although independent from each other, the two brains are strictly connected to each other and exchange an enormous amount of messages that travel in both directions. The effects of stress on digestive functions (brain-gut axis) has long been known, while on recently data have been produced on the effects that visceral events exert on cerebral activities (gut-brain axis), apart from symptom perception. Both brains are necessary for life, but messages rising from the gut to the brain are 8-9 times greater than those that move from the brain to the gut. Fortunately, most of these messages never gets to the cortex and therefore to the awareness level. Only when these signals get higher than perception threshold they are perceived as symptoms, but if lower than this threshold (and therefore unperceived) visceral signals influence big brain activities, as confirmed by beneficial effects of probiotics on depression. Visceral hypersensitivity is more pronounced in females than in males, similarly to what observed with cutaneous and somatic sensibilities. This is also confirmed by the higher prevalence

of pain-related syndromes in females compared with males, including abdominal pain, pelvic pain, dysmenorrhea, dysuria, headache/migraine, fibromyalgia.

## IRRITABLE BOWEL SYNDROME

**Vincenzo Stanghellini**

*IRCCS S. Orsola, University of Bologna, Italy*

Gynecologists should be interested in understanding gastrointestinal (GI) disorders for different reasons: 1) the bowel is an anatomically important neighbour of the uro-gynecological organs; 2) it harbours 1500 mg of microbiota that represent the only source of non-sexually transmitted uro-gynecological infections; 3) digestive and gynecological disorders often overlap and may share common pathophysiological mechanisms; 4) pain of intestinal origin may mimic gynaecological conditions, thus causing major clinical mistakes; 5) intestinal diseases and proctological surgeries may be associated with relevant sexual disturbances in substantial proportions of cases. Irritable bowel syndrome (IBS) is one of the most common gastrointestinal disorders in which abdominal discomfort or pain is associated with a change in bowel habits, and with features of disordered defecation (constipation, or diarrhea, or alternating constipation and diarrhea). It has long been considered an expression of somatisation in neurotic, hypochondriac women (due to the high prevalence of females among affected individuals), but evidence has accumulated over the last decades demonstrating it is an organic (or rather micro-organic) disease. Induced by well-characterized cellular and molecular mechanisms. In fact, a number of recent studies have provided microscopic and molecular evidence of immune cell infiltration (i.e., T cells and mast cells) and activation (e.g., release of cytokines, histamine, proteases) in the intestinal mucosa of IBS patients. This immune activation has been demonstrated to be involved in altered bowel physiology, increased visceral sensitivity and symptom generation. Compelling evidence suggests that gender plays an important role in the epidemiology, pathophysiology, and susceptibility to pharmacological agents in IBS patients. Sex hormones are thought to play a key role in gender-dependent features of IBS and to influence the immune system. Particularly, mast cells express progesterone and estrogen receptors and experimental evidence suggests that these hormones have a strong influence on mast cell function in the intestine. Furthermore, IBS patients often complain of extra-digestive syndromes suggesting potential common pathophysiological mechanisms. Among these, urogenital disorders are particularly frequent in IBS patients compared to what observed in the general population. Over 80% of IBS patients reports sexual dysfunctions, 50% have chronic pelvic pain, 10-20% dysmenorrhea, and 50% dysuria. Also, fertility seems to be decreased in both male and female IBS patients. Similarly, other extra-digestive diseases have also been found to be particularly frequent in IBS patients, including fibromyalgia (26-65%), headache (34-72%), migraine (three times higher than in controls). Whether and to which extent the concomitant expression of these pathological conditions in the same individuals represents common underlying pathophysiological mechanisms such as abnormal immunological responses to different stimuli represents an important field for future research.

## ANTEPARTUM ULTRASOUND IN LABOR WARD

**Boris Tutschek, Switzerland**

Traditionally, the assessment and management of a woman in labor is based upon clinical findings. The diagnosis of

arrest of labor and decisions regarding the timing or type of intervention rely mostly on digital evaluation of cervical dilatation and fetal head station and position. However, clinical examination of head station and position is inaccurate and subjective, especially when caput succedaneum impairs palpation of the sutures and fontanels. The use of ultrasound has been proposed to aid in the management of labor. Several studies have demonstrated that ultrasound examination is more accurate and reproducible than clinical examination in the diagnosis of fetal head position and station and in the prediction of arrest of labor. Ultrasound examination can, to some extent, distinguish those women destined for spontaneous vaginal delivery and those destined for operative delivery. Furthermore, there is growing evidence that ultrasound in labor may predict the outcome of instrumental vaginal delivery. Ultrasound in labor can be performed using a transabdominal approach, mainly to determine head and spine position, or a transperineal approach, for assessment of head station and position at low stations. Several quantitative sonographic parameters have been proposed to assess head station

## DUO-STIMULATION

**Filippo Maria Ubaldi, Italy**

The technical improvements in IVF (e.g. blastocyst culture, single embryo transfer (SET), cryopreservation of oocytes/embryos, preimplantation genetic testing for aneuploidies (PGT-A), freeze-all) allowed the implementation of non-conventional controlled ovarian stimulation (COS) protocols for oncologic and poor prognosis patients in IVF. However, the current theory states that several waves of follicular recruitment might arise throughout the ovarian cycle this opened the possibility of non-conventional COS protocols outside the fertility preservation context. Beyond the random start approach, at least three more non-conventional COS protocols involve a stimulation starting in the luteal phase of the ovarian cycle: late follicular phase stimulation (late-FPS), luteal phase stimulation only (LPS-only) and double stimulation in the same ovarian cycle (FPS plus LPS, or DuoStim). These non-conventional COS protocols have been adopted across the last decade to treat poor prognosis women and/or patients of whom time to oocyte retrieval is critical. Using LPS in the same ovarian cycle 5 days after ending FPS (i.e. DuoStim), represents the most promising non-conventional protocol to treat poor prognosis women, as consistently reported from several groups worldwide. Moreover this protocol has been successfully adopted also for fertility preservation where the time is crucial. The rationale of DuoStim approach is to increase the number of oocytes and embryos available per menstrual cycle in all patients where obtaining competent oocytes is an urgent task for malignant diseases or other medical indications and in patients with advanced maternal age and/or reduced ovarian reserve such as patients fulfilling Bologna Criteria. The number of oocytes retrieved, in fact, together with the age of the patient is one of the most important factor to predict the live birth of a healthy baby. Based on the studies already published, DuoStim protocol is an alternative option for increasing number of MII oocytes retrieved and of the blastocysts obtained in short time frame increasing the efficacy of an IVF procedure without compromise the oocytes competence coming from anovulatory waves. Indeed exogenous gonadotropins started in follicular or in luteal phase, seems not significantly modify the fertilization and blastulation rate as well as the likelihood of aneuploidy embryos in patients undergoing COS. Observation studies showed that DuoStim is not superior to two conventional COS protocols in terms of CLBR per ITT. However, DuoStim strategy lessens the patient drop-out rate,

which is highly likely after a failed attempt with conventional COS. On the other hand, LPS provides these patients with a higher chance to obtain and transfer an euploid blastocyst in the same ovarian cycle. Cost-benefit analyses are required from future trials. However, until such evidences can be produced, the autonomous informed choice of the patients to undergo a DuoStim protocol should not be questioned, especially after a thorough and careful counseling of its pros, cons, and putative alternatives. Finally, DuoStim protocol is confirmed a feasible and efficient approach also from clinical, obstetric and perinatal perspectives, targeted at patients who need to reach the transfer of an euploid blastocyst in the shortest timeframe. These results encourage additional clinical studies and research to further personalize COS in specific populations of patients, many of whom may benefit from non-conventional protocols. This evidence should be confirmed in future RCT, long-term follow-up of the babies born after LPS are advisable.

## STOP RESECTING THE UTERINE SEPTUM

Fulco van der Veen, *Netherlands*

For nearly a century, surgical correction of the septate uterus, first by transabdominal laparotomy and hysterotomy and more recently by hysteroscopy has been the standard procedure in women with a uterine septum. The simplistic but intuitively appealing reasoning behind resecting the septum has always been the assumed disturbed implantation within a septate uterus, but actual data on the pathophysiology of the intrauterine septum is extremely limited and a plausible biological mechanism underpinning the medical intervention has not been identified. Until recently, the existing evidence underpinning surgical removal was incredibly meager. A Cochrane review published in 2017 could not identify a single randomized controlled trial on reproductive outcomes after surgery compared to an expectant management. In 2020 new data of more robust research became available. A large international multicentre cohort study was published, performed in the Netherlands, the USA and the UK, including women with a septate uterus and a wish to conceive. 257 women were ascertained on the basis of a history of subfertility, pregnancy loss or preterm birth, but they could also have been identified during a gynaecological examination, an ultrasound in pregnancy or during a caesarean section. The women were diagnosed with a septum uteri between 1981 and 2018; the diagnosis was made by the treating physician according to the classification system at that time. 151 women underwent septum resection and 106 women had expectant management. 80 of the 151 women who had surgery (53.0%) had at least one live birth, compared to 76 of the 106 women who had expectant management (71.7%) (HR 0.71 (95% CI 0.49-1.02)). Also, in 88 women with a history of subfertility, there were no differences in reproductive outcomes after adjustment for possible confounders like age, BMI, smoking, ethnicity, country, classification, diagnostic procedure, pregnancy loss, preterm birth and previous live birth (HR 0.90 (95% CI 0.63-1.28)). On the issue of safety, there were complications in seven women (4.6%); in three women there was a uterine perforation, in one woman the maximal allowed amount of intravasation was reached, and in three women there was more blood loss than was deemed acceptable. At the time of writing this abstract, the TRUST study, in which 80 women were randomly allocated to hysteroscopic septum resection or expectant management between 2010 and 2018, is under review. The intention to treat analysis (ITT) showed that 12 of 39 women allocated to septum resection (31%) had a live birth, compared to 12 of 39 women allocated to expectant management (35%) (RR 0.88 (0.47-1.65)). The results of a per

protocol analysis were completely in line with the ITT. With the sample size it was possible to detect an improvement of live birth from 35% to 70% with surgery, which was expected based on the existing literature at the start of the study. To detect a smaller improvement of 10% in live births, for example from 35% to 45%, new studies would need to recruit at least 752 women. Any effort to confirm or refute the results of this trial would thus need a worldwide, dedicated and adequately resourced collaboration. Such an enterprise is unlikely to be feasible, especially if one considers that the only other randomised controlled trial comparing septum resection with expectant management carried out in the UK was forced to stop because of poor recruitment; six patients in a recruitment period of three years (Pilot randomised controlled trial of hysteroscopic septum resection, ISRCTN28960271). For decades, the recommendation worldwide has been to perform septum resection based on low graded evidence. The procedure is widely offered, but is associated with financial costs for society, healthcare systems or the patients themselves. Both studies discussed above unequivocally do not reveal any improvements in reproductive outcomes, thereby questioning any rationale behind surgery. It has to be stopped.

## UNEXPLAINED INFERTILITY: WHAT DO WE DO?

Fulco van der Veen, *Netherlands*

Unexplained infertility is a typical example of an idiopathy as it is a condition with an unknown cause or mechanism. None of the available treatment options are therefore based on any understanding of the biological mechanisms involved. Currently, three options are available; continuing natural conception, intra uterine inseminations (IUI) and in vitro fertilization (IVF). To decide which option to recommend, it is important to realize that couples attempting to become pregnant have a new chance to conceive every month again, and that each couple has a ~ constant monthly chance to conceive, but between couples chances vary widely. This means that the most fertile couples conceive first, leaving progressively less fertile couples in the pool of not (yet) pregnant couples. Over time, the population of our patients thus changes from a heterogeneous group with variable prognoses on natural conception into a more homogenous group with an ever-increasing worse prognosis. This implies that the prognostic profile of the couples we see and treat is of paramount importance and this in turn means that we cannot apply IUI or IVF in couples with unexplained infertility without first determining their actual prognosis on natural conception. Models that are able to do so currently exist and have been validated. So far, only 2 randomized controlled trials have integrated prognosis on natural conception into their comparison on IUI versus expectant management. One trial included couples with an intermediate prognosis on natural conception and found no effect of IUI. The second trial included couples with a poor prognosis and found a large benefit of IUI. To test the hypothesis that the difference in results could be explained by the difference in prognosis, a prospective cohort study followed couples with unexplained infertility after expectant management in which a subset of couples started IUI at some point of follow up. A lower initial prognosis of natural conception was associated with a larger relative and absolute benefit of IUI. On IVF there are no trials taking into account the prognosis on natural conception. A large cohort study matched couples with unexplained infertility undergoing IVF or expectant management for female age, duration of subfertility and parity. It appeared that IVF increased the average one-year chance of conception compared to expectant management. The factors affecting effectiveness were female age, duration of subfertility and

primary versus secondary subfertility. These data and a subgroup analysis performed in a network meta-analysis comparing IUI and IVF with expectant management show that IUI and IVF only contribute to an increase in live birth rate in couples with a poor prognosis on natural conception. IUI in couples with unexplained infertility should thus only be used after careful assessment of their prognosis relative to their chances after extended natural conception at various time points. IVF should in view of costs, burden and invasiveness only be used after failed IUI.

## VAGINAL MICROBIOME: A NEW FRONTIER INTO ANTIBIOTIC RESISTANT SUPERBUGS

Gary Ventolini, USA

The genital tract including the vaginal microbiome embodies 9% of the total women's microbiome. Up-to-date advances in vaginal microbiome research have revealed that *Lactobacilli* products and their biofilms will let us to address severe medical conditions. Specially those associated to pathogen biofilm producers and antibiotic resistant microorganisms so called "Superbugs". One of them, *Pseudomonas aeruginosa* frequently colonizes patients with severe infected burn wounds causing sepsis, multiple organ failure and death worldwide. *Lactobacilli* deploy a defensive role by interfering with Superbugs growth and/or adhesion. Biofilm formation by *Lactobacilli* in vivo was reported from uninfected vaginal samples. Additionally, *Lactobacilli* spp. has shown in vitro to inhibit the growth and biofilm development by *P. aeruginosa*. Even though more significantly, a recent account by our research team showed in an animal model that 20x concentrated supernatant from *Lactobacilli gasseri* inhibited the growth of *P. aeruginosa*, prevented its Biofilm formation and partially eliminated already established biofilms. These results suggest a likely use of *L. gasseri* in preventing sepsis from *P. aeruginosa* infection in severely burned and immunocompromised Patients. We will be discussing these latest reports and discoveries regarding *Lactobacilli* products and biofilms. They unquestionably will permit us to appropriately address these and other serious Superbugs associated medical conditions and to restore health and enhance quality of life across men's and women's lifespan.

## THE EFFECT OF OVARIAN STIMULATION ON PLOIDY STATUS

Willem Verpoest

Centre for Reproductive Medicine, Universitair Ziekenhuis Brussels, Belgium

The mechanism of aneuploidy in human embryos is still under research and new insights are still gained, yet it is clear that the aneuploidy rate is relatively high compared to other mammalian species and is age-dependent (Webster and Schuh, 2017). A number of studies in human oocytes have suggested that aneuploidy rates in embryos may be altered by ovarian stimulation protocols employed in IVF, as well as patient estradiol ( $E_2$ ) levels and the number of retrieved oocytes, even in young patients (Munne et al., 1997, 2006; Soares et al., 2003; Katz-Jaffe et al., 2005; Baart et al., 2006). High intensity ovarian stimulation for IVF and ICSI potentially induces aneuploidy, due to errors at different levels, including first and second meiotic oocyte divisions, and genomic imprinting disorders (Sato et al., 2007). An increased oocyte yield has been associated with increased aneuploidy rate (Haaf et al., 2009), whereas other groups have not confirmed this finding (Gianaroli et al., 2000). A number of authors suggested that milder stimulation or absence of stimulation potentially reduces aneuploidy rates in embryos (Nargund et

al., 2001; Pelinck et al., 2005). The proportion of aneuploidy in embryos is reduced by milder ovarian stimulation, as illustrated by Baart et al. in a study where 111 patients under the age of 38 were randomised to have either a conventional stimulation protocol using pituitary suppression by a gonadotrophin-releasing hormone (GnRH) agonist, compared to a mild stimulation protocol using a GnRH antagonist. The study was terminated prematurely because of a significantly lower abnormality rate of 35% in the mild stimulation compared to 50% in the conventional stimulation group (Baart et al., 2007). A more recent study by Rubio et al., compared two subsequent stimulation protocols in terms of embryo aneuploidy rate in a cross-over study of 32 young oocyte donors. In the group of non-cancelled milder stimulations, a significantly increased fertilisation rate and increased ploidy rate was observed (Rubio et al., 2010). Other studies have not been able to establish induction of chromosomal abnormalities in inseminated oocytes by superovulation (Gras et al., 1992). However, there are few data available on the chromosomal abnormality rate in embryos derived from natural or unstimulated cycles. A small observational study reported an aneuploidy rate of 36.4% in a series of 30 unstimulated cycles, of which 11 ended up having PGS performed (Verpoest et al., 2008). The ESHRE pilot study in which aCGH of polar bodies was carried out suggests that ovarian stimulation may induce meiotic abnormalities, as observed in the small series of PGT-A with aCGH that was performed to assess the feasibility of a large RCT (Geraedts et al., 2011). A prospective cohort study published in 2012 by Labarta et al. compared the aneuploidy rate by cleavage stage FISH analysis between unstimulated cycle IVF embryos and embryos conceived after conventional stimulation and did neither show a significant difference between the two groups nor an intrasubject difference (Labarta et al., 2012). A prospective observational comparative study published in 2019 by Hong et al. compared the aneuploidy rate analysed by quantitative PCR (qPCR; study period 2013-2015) on trophoctoderm biopsy material and did not show a significant difference in aneuploidy rate between embryos conceived from oocytes retrieved following dual trigger by exogenous hCG and GnRH agonist (43.5%) compared to embryos conceived after conventional oocyte stimulation in a historical cohort (36.7% aneuploidy rate) (Hong et al., 2019). There is currently no evidence suggesting a relation between ovarian stimulation for IVF and increased aneuploidy rates.

## MEIOSIS GENE DYSFUNCTION AS A CAUSE OF INFERTILITY

Willem Verpoest

Centre for Reproductive Medicine, Universitair Ziekenhuis Brussels, Belgium

It is estimated that 10-15% of couples are affected by infertility during reproductive age and this seems to be equally distributed among males and females (Esteves et al. 2012). For many of these cases, the cause of infertility cannot be determined, suggesting that genetic alterations could be responsible. For example, 50-80% of cases diagnosed with primary ovarian insufficiency (POI) remain idiopathic (Laissue, 2015). Conversely, in 80% of men with non-obstructive azoospermia the cause remains unknown (Lee et al., 2011). Meiosis is an essential process of gamete formation and it is expected that genetic disruptions in genes responsible for this process have a considerable impact on fertility in general. Clinical expression of meiosis genes is apparent at different levels varying from ovarian reserve, over ovarian response to oocyte maturity and activation. Meiosis gene mutations may therefore lead to a number of clinical pathologies such as primary ovarian insufficiency (POI), but

also to insufficient oocyte maturation and low fertilisation rate. However, in humans, only a handful of gene mutations have been discovered which have been shown to lead to aberrant meiosis and infertility (Lee et al. 2011; Gheldof *et al.*, 2019). There are a number of treatment options in suspected meiosis dysfunction. At a reproductive young age the female patient, informed about a potential pathological reproductive function, has the possibility to cryopreserve gametes or ovarian tissue for fertility preservation purposes. It will allow the patient to make decisions regarding personal reproductive plans or family planning, as well as to suggest alternative treatments such as gamete donation if the meiosis dysfunction is significantly affecting the reproductive prognosis. At a stage where the patient decides to plan a family, several ovarian stimulations strategies are available to address the folliculogenesis, oocyte maturation and at the level of the laboratory the embryo development by using different techniques and cultures.

#### **WHAT HAPPENS AFTER THE STAR AND ESTEEM STUDIES TRIALS THAT HAVE FAILED TO SHOW BETTER RESULTS? SHOULD WE STOP PROPOSING PGT-A TO PATIENTS? SHOULD WE CHANGE OUT CLINICAL ATTITUDE TOWARDS THE TEST? NO**

**Willem Verpoest**

*Centre for Reproductive Medicine, Universitair Ziekenhuis Brussels, Belgium*

No: Incremental awareness

As with all developments in science in general and medicine in particular, progress is made through research and incremental awareness of the possibilities and limitations of new techniques. Admittedly, it has taken quite some time to realise that preimplantation genetic screening by cleavage stage biopsy and FISH for a limited number for chromosomes could implausibly improve cumulative live birth rates. The studies that established this were unnecessarily late and limited in design. Furthermore, when not performed to the best standards, PGS could reduce CLBR by deselecting embryos that did not survive the biopsy, prolonged culture or cryopreservation techniques at the time (Mastenbroek et al., 2007).

With the advent of whole genome analysis techniques, improved blastocyst culture, vitrification and trophectoderm biopsy techniques, the interest for the newly termed preimplantation genetic testing for aneuploidy (PGT-A) (Zegers-Hochschild et al., 2017) self-evidently increased. In contrast to the PGS studies in the mid 2000ies, a number of investigators and authorities were quicker to attempt analysis of the new complete chromosome complement analysis of embryos. This included the ESTEEM trial initiated by ESHRE (Verpoest et al., 2018), the trial by Rubio et al., 2017 and the Single Transfer of an Euploid Embryo (STAR) trial (Munné et al., 2019).

What happens after the STAR and ESTEEM studies trials that have failed to show better results?

The answer to this question is straightforward: none of the studies performed so far was able to establish superiority and was neither sufficiently powered to assess non-inferiority. The STAR trial analysed exclusively the first embryo in both study arms hence a cumulative analysis was not made. The ongoing implantation rate for PGT-A of the first embryo above 34 years of age was significantly different. Other studies

looked at cumulative live birth rate and logically did not show superiority as PGT-A can never improve an embryo hence cumulative results will always be similar. What happens after these studies is increasing knowledge on the mechanism of intermediate copy number and the factors that affect it, the awareness that some mosaic embryos lead to healthy children however that more data are needed to establish which types of intermediate copy number embryos should be allowed to transfer. Ideally this should be analysed by non-selection studies.

Should we stop proposing PGT-A to patients?

No. IVF centres that are not able to perform PGT-A and associated embryo culture, biopsy and cryopreservation techniques to the maximum standard should indeed not propose this technique to the patients. It has become obvious from the different PGT-A studies mentioned before that the effect of the IVF lab and genetic lab is considerable. Furthermore, genetic interpretation of the PGT-A results should equally be performed to the highest standards to avoid deselecting potentially viable embryos. Finally, the counseling of the patients regarding the results, and more specifically mosaic results, should be in the hands of experienced clinicians in order to avoid once more deselecting potentially viable embryos. If these conditions are met, PGT-A is a valuable and safe technique.

Should we change out clinical attitude towards the test?

Yes. All too often it is the patient who is not sufficiently informed and refuses a mosaic embryo to be transferred. We should be aware that intermediate copy number, as we may want to use instead of the term mosaic, can lead to healthy children, be it with a lower implantation rate and higher miscarriage rate and taking into account that further research is needed on the true risks of intermediate copy number in the human. We also need to be aware that the lab report is subject to external factors such as lab techniques, biopsy techniques, DNA amplification methods, threshold levels for calling mosaicism as well as data analysis. Last but not least, we need to properly counsel the patient about the true value of PGT-A in avoiding miscarriages and aneuploidy in embryos hence offspring.

#### **IS LASER TREATMENT FIRST LINE CHOICE FOR GENITOURINARY SYNDROME OF MENOPAUSE (GSM)?**

**Zdenko Vizintin**

*Fotona, Stegne 7, 1000 Ljubljana, Slovenia*

To present the safety and efficacy of lasers (in particular the non-ablative ErYAG laser) for minimally invasive non-surgical gynecological treatment of Genitourinary Syndrome of Menopause (GSM). **Introduction:** Non-surgical minimally invasive gynecological treatments represent one of the fastest growing segments on the energy based devices (EBD) market offering applications in rather wide range of indications, from treatment of vaginal laxity to urinary incontinence, genitourinary syndrome of menopause, pelvic organ prolapses, lichen sclerosus and others. In spite of many clinical studies executed and published, showing good results and very low level of adverse effects, there are still a lot of doubts and criticism considering clinical evidence of efficacy and safety of these treatments. In this talk we are analyzing the efficacy and safety of lasers for treatment of GSM. **Methods:** Energy based devices used for the treatment of

GSM are mostly lasers and radiofrequency devices, but there are also a few high intensity ultrasound devices present on this market. Due to the time limitation we are concentrating just on laser solutions – particularly on non-ablative vaginal erbium laser (VEL). An overview of published clinical studies is given showing the safety as well as the efficacy assessed with various objective and subjective tools. Also, a worldwide survey among the users of non-ablative erbium laser technology was conducted with the aim to establish the safety and efficacy of intra-vaginal use of this technology and the results of this survey are presented as well. **Results:** In two studies the VEL treatment was compared with topical estriol treatment for management of GSM. It has been shown that the laser treatment, in comparison to topical estriol, provides significantly greater and longer-lasting improvement in maturation value, pH and the signs and symptoms of vaginal atrophy. Similarly, assessment of dryness, dyspareunia and Vaginal Health Index Score (VHIS) showed that the Er:YAG treatment is significantly better than vaginal estriol. Other studies showed that VEL treatment is very efficacious and safe for hormone receptor-positive breast cancer patients and breast cancer survivors for which the systemic postmenopausal hormone use is currently contraindicated. **Conclusions:** Based on the existing body of evidence and clinical data, we believe that laser therapy for GSM is efficacious and safe and that considering its minimal invasiveness and very low level of side effects could be future treatment of choice for GSM, especially for hormone receptor-positive breast cancer patients and breast cancer survivors.

#### WHEN ONLY ONE EMBRYO IS AVAILABLE, IS IT BETTER TO TRANSFER ON DAY 3 OR TO GROW ON?

Joyce S. Xiao, Martin Healey, Alon Talmor, Beverley Vollenhoven, Australia

**Research question:** In patients with only one embryo on Day 3 post-IVF treatment, does transferring the embryo into the uterine environment achieve a higher pregnancy rate than growing the embryo on with a plan to transfer at Day 4–6? **Design:** This was a retrospective cohort study conducted in patients with only one viable embryo on Day 3 post-IVF treatment. Data were extracted from a standardized IVF database and included 1384 women who fulfilled this study's selection criteria. Outcomes of these embryos were followed up and stratified into two groups: embryos transferred on Day 3 and those grown on to Day 4–6. Pregnancy rate (biochemical and clinical) and live birth rates were analysed with logistic regression and adjusted using a parsimonious model for baseline patient characteristics. **Results:** Biochemical pregnancy (16.7% versus 9.5%, odds ratio [OR] 1.9,  $P = 0.001$ ), clinical pregnancy (14.7% versus 6.8%, OR 2.35,  $P < 0.001$ ) and live birth rates (9.7% versus 4.4%, OR 2.37,  $P = 0.002$ ) were significantly higher in the Day 3 group than those in the group grown on to Day 4–6. These differences were still significant after adjusting for potential confounders (adjusted OR 2.60, 3.71, 4.08, respectively,  $P < 0.001$ ). **Conclusions:** These findings support Day 3 cleavage-stage embryo transfer instead of growing on to Day 4–6 for blastocyst-stage transfer when only a single embryo is available.

#### DEVELOPMENTAL POTENTIAL OF ANEUPLOID HUMAN EMBRYOS CULTURED BEYOND IMPLANTATION

Magdalena Zernicka-Goetz, UK and Bailey Weatherbee, UK

Aneuploidy, the presence of an abnormal number of chromosomes, is a major cause of pregnancy loss in humans.

However, the developmental effects of specific aneuploidies are not well understood. In order to interrogate these consequences, we first examined a large dataset of *in vitro* fertilized human embryos to assess the prevalence of individual single chromosome aneuploidies and their respective quality and ability to reach the blastocyst stage. While timing and morphological quality differed, all aneuploid embryos were able to successfully develop to the blastocyst stage. We selected a set of specific, common aneuploids that showed minimal differences compared to euploid embryos during pre-implantation development for further investigation. Using our recently developed system, we were able to, for the first time, culture embryos harboring these specific whole-chromosome aneuploidies beyond implantation. We show that trisomy 15 and trisomy 21 human embryos develop similarly to euploid embryos at these stages, however monosomy 21 embryos exhibit high rates of developmental arrest and trisomy 16 embryos display a trophoblast-specific hypo-proliferation phenotype. Using human embryonic and trophoblast stem cells, we show that this tissue-specific effect can be ascribed to increased levels of the adhesion protein E-CADHERIN, which is encoded on chromosome 16. We show that increased E-CADHERIN expression results in premature terminal differentiation and cell cycle arrest in trophoblast cells. We identify three cases of mosaicism in embryos previously diagnosed as fully aneuploid through pre-implantation genetic testing. This may reflect misdiagnoses or subsequent mitotic non-disjunctions which occurred after the blastocyst stage. These results represent the first detailed analyses of human aneuploid embryo development beyond implantation.

#### PERSISTENT INFECTIONS IN THE EARLY PERIOD OF LIFE AS RISK FACTORS FOR DISEASES DECADES LATER

Harald zur Hausen and Ethel-Michele de Villiers  
Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany

Based on epidemiological data, we suspected approximately 20 years ago the involvement of infections in the etiology of colon and breast cancers. Initially, we based this on a geographic correlation of incidences for these two cancers on a global scale. We also noted a remarkable geographic coincidence with areas of high consumption of beef and dairy products of Eurasian cattle. These observations stimulated us to search for potential infectious pathogens in serum and milk products of these animals. Up to now, we isolated a large number of small single stranded circular DNA molecules from these materials. Their relationship to specific plasmids of *Acinetobacter* bacteria permitted their molecular characterization into two clades, labeled as "bovine meat and milk factors (BMMFs 1 and 2)". Analysis of human materials provided a surprising result: we did not find their DNA in tumor cells from colon or breast cancer. After development of monoclonal antibodies against a protein derived from the major open reading frame (*Rep*) of a BMMF1 genome, we observed specific staining in *lamina propria* cells, directly adjacent to *Lieberkühn's crypts*, from which colon polyps and colon cancer arise. The staining of peri-glandular cells in breast cancer biopsies - with negative results in breast cancer cells. Two other observations were obvious in surgically removed colon and breast tissues: Foci of stained cells also contained CD68-positive macrophages, revealing the presence of 8-hydroxyguanosine as an indication for the function of reactive oxygen molecules. Sugars, specifically present in human milk (2'- and 3'-fucosyllactoses and disialyl-tetraoses) prevent BMMF infections by blocking their binding to BMMF receptors. Similarly, stressing the importance of

induced inflammatory events, non-steroidal anti-inflammatory drugs (aspirin, ibuprofen and others) reveal a preventive function. An interesting other aspect became apparent: in follow-up studies, long-lasting immunosuppressions, e.g. after organ transplantation or chronic human immunodeficiency virus (HIV) infections, have a protective effect for breast, colon, and prostate cancers. These observations were the basis for the hypothesis that colon and breast cancers originate from an *indirect infectious carcinogenesis*, similar to cancers arising from *hepatitis C*, *helicobacter pylori*, and parasitic infections (*Schistosoma*, *Opisthorchis*, *Clonorchis*). The cancer cells remain negative for genes of the respective agents, yet reactive oxygen or nitrogen molecules, produced by chronic inflammation, induce random mutations in the adjacent glandular cells. Premalignant and subsequent malignant lesions are the consequence of hits in more than one specific “*driver*” gene of replicating cells. Except for genetic predispositions, this explains the very long latency periods between primary infection (commonly during and after the weaning period) and the respective cancer formation (in average 30 to 60 years later). A model has been established which reflects the present understanding of the etiology of colon cancer (probably also applicable for breast cancers). It becomes apparent that specific indirectly acting infections (here as a zoonosis acquired early in life) via chronic inflammations will influence future considerations of preventive and therapeutic approaches to several common human cancers. Possibly this will also become important for chronic neurological and autoimmune diseases, childhood diabetes mellitus and early onset of arteriosclerosis.

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## E-POSTER ABSTRACTS

### ART/IVF

#### PREDICTORS OF LIVE BIRTH FOLLOWING A SINGLE EMBRYO TRANSFER IN FRESH AND FROZEN IVF/ICSI CYCLES

Devini Ameratunga<sup>1,2,3</sup>, Ebenezer Owusu

Adjah<sup>3</sup>, Akwasi Amoako<sup>1,2,3</sup>

<sup>1</sup>Fertility, City Fertility, Brisbane, Australia

<sup>2</sup>Obstetrics & Gynaecology, Royal Brisbane & Women's Hospital, Brisbane, Australia

<sup>3</sup>Medicine, University of Queensland School of Medicine, Brisbane, Australia

**Problem statement:** Prediction models for in-vitro fertilization (IVF) success assist with individual counselling, better tailored patient protocols and guides on which embryos to transfer. We aimed to compare accuracy of machine learning algorithms to predict live births following single embryo transfers. **Methods:** The study population consisted of 19,927 frozen and fresh single blastocyst transfers in the City Fertility Centre database from January 2005 to January 2020. Independent variables including age, BMI, smoking status, cause of infertility, and embryo assessment characteristics were used to construct classification algorithms (logistic regression and support vector machine) to predict IVF outcomes (clinical pregnancies, live births). The models were trained on the training set (n=15,941) with 10-fold cross-validation and evaluated on the test set (n=3,986). **Results:** Logistic regression algorithm algorithms based on specific patient characteristics such as age, BMI, and smoking status were better at predicting IVF outcomes (clinical pregnancy rates, live births) with a Brier score of 0.177 (range 0 to 1, representing perfect to imperfect predictions, respectively), suggesting that the machine predictions were closely associated with actual outcomes. **Conclusion:** This study has demonstrated the applicability of predictive models to estimate the success of IVF treatment at the embryo-level based on specific characteristics. It also shows that validated machine learning models have an advantage. This model could be used to inform both patient and clinician regarding the estimated likelihood of treatment success, assist in adjustment of treatment strategy as well as assist the embryologist to select the most appropriate embryo for transfer.

#### EMBRYO QUALITY AND CHROMOSOMAL STATUS. IS THERE RELATIONSHIP BETWEEN BOTH?

Silvia de Frutos<sup>1</sup>, Marta Ariza<sup>1</sup>, Maria Gaytan<sup>1</sup>, Eva Maria Martinez<sup>1</sup>, Maria Del Carmen Nogales<sup>1</sup>, Fernando Bronet<sup>1</sup>, Maria Jose De Los Santos<sup>2</sup>, Mireia Florensa<sup>3</sup>

<sup>1</sup>Preimplantation Genetic Department, IVI RMA Madrid, Madrid, Spain

<sup>2</sup>IVF, IVI RMA Valencia, Valencia, Spain

<sup>3</sup>IVF, IVI RMA Barcelona, Barcelona, Spain

**Problem statement:** To find a correlation between embryo morphology grade and chromosomal status. **Methods:** A retrospective, observational and multicenter study that include all PGT-A and PGT-SR cycles performed from May 2016 to February 2019 in IVI Madrid, IVI Valencia and IVI Barcelona. A total of 18513 embryos were biopsied on day 5 or day 6 of development and analyzed through Next Generation Sequencing (NGS). We grouped the embryos in six different groups regarding blastocyst quality and the biopsy day (Table 1). Statistical program SPSS was used to find if there were significant statistical differences among analyzed groups. All biopsied blastocysts were hatching or hatched. Blastocysts were divided as followed: 880 in Group 1 (AA), 1730 in Group 2 (AB/BA), 8134 in Group 3

(BB), 7890 in Group 4 (BC/CB/CC) and 118 in Group 5 (AC/CA) and 10 in Group 6 (CA).

**Results:** Figure 1: Euploid embryo rate depending on the morphology and biopsy day

Biopsy day	MORPHOLOGY GROUP					
	1	2	3	4	5	6
Day 5	47.2% (n=694)	48% (n=1331)	38% (n=5984)	21.3% (n=4213)	20% (n=76)	100% (n=4)
Day 6	61.2% (n=178)	42.7% (n=389)	33.7% (n=2043)	18% (n=3552)	17.5% (n=40)	100% (n=6)
p value	0.0009	>0.05	0.0005	0.0003	>0.05	>0.05

**Conclusion:** Day 6 blastocysts with average quality show a decrease in euploid embryo rate when comparing to similar quality blastocyst at day 5. On the other hand, good quality blastocysts at day 6 do not have lower likelihood of having euploid embryos than good quality blastocyst at day 5. The data also suggest that embryos reaching to blastocyst stage with good quality but slower, those biopsied on day 6, could have even less aneuploidy rates.

#### AUTOLOGOUS INSEMINATIONS ARE LESS EFFECTIVE THAN USING DONORS

Marta Armas Roca<sup>1</sup>, Leticia Maya Merino<sup>1</sup>, Jose Alberto Tabares Concepcion<sup>2</sup>, Lourdes Roldan Gutierrez<sup>1</sup>, Nelda Benitez Castillo<sup>1</sup>, Maria Alejandra Santana Suarez<sup>1</sup>, Monica Alvarez Sanchez<sup>1</sup>

<sup>1</sup>Ginecología y Obstetricia, Complejo Hospitalario Insular Materno Infantil De Canarias, Las Palmas De Gran Canaria, Spain

<sup>2</sup>Análisis Clínico, Complejo Hospitalario Insular Materno Infantil De Canarias, Las Palmas De Gran Canaria, Spain

**Problem statement:** The literature provides clinical results in assisted reproduction techniques in heterosexual couples. Not so, in single women, homosexuals and heterosexual couples who require donor semen. The objective of this study is to analyze the epidemiological and reproductive characteristics in the different groups. **Methods:** Retrospective cohort study in a tertiary hospital that includes all artificial inseminations (IUI): heterosexual couples using autologous (A-HC), heterosexual using donors (D-HC), single woman (SW) and homosexual (LC) performed between 2008 and 2019. A total of 2448 IUI were included. **Results:** The mean age of the A-HC was 33.7 ± 3.5 and that of the donor was 33.5 ± 3.9 (p 0.01). The mean FSH dose was higher in the A-HC group (672 ± 593) than in the donor (564.7 ± 393) (p 0.001). The A-HC presented larger follicles with respect to the donor groups (1.43 vs. 1.37) (p 0.03). We did not obtain significant differences in Body mass index (BMI), days of stimulation and endometrial thickness. In the D-HC group there were more multiple pregnancies 11 (9.2%) compared to A-HC 38 (6.9%), single woman 38 (6.9%) and homosexual 3 (3.5%) (p 0.001). A live birth rate per cycle is more frequent in the D-HC group (16.52%) followed by homosexual (16.52%), single woman (14.82%) and A-HC (9.3%) (p 0.001). There are more miscarriage/ ectopic in the single woman group (24.4%), followed by D-HC (18.3%), A-HC (19.1%) and homosexual (10.5%) (p 0.001). In the multivariate analysis of logistic regression for live newborn, it had a prognostic impact belonging to the different groups, as well as the BMI and the age of the patient. **Conclusion:** This study provides evidence of equivalent clinical results in the three population groups treated with donor semen while the success rate of autologous is significantly lower. The multivariate analysis identified three factors that were really relevant to the result: population group to which the patient belonged, the BMI and the age of the patient.

## ACUPUNCTURE AND FEMALE INFERTILITY: A LITERATURE REVIEW OVER STUDIES PUBLISHED IN THE LAST 5 YEARS

Tatiana Branco Vaz<sup>2</sup>, Joao Cruz<sup>1</sup>, Domingos Branco Vaz<sup>3</sup>, Diogo Calado<sup>1</sup>

<sup>1</sup>Biomedical Sciences, School of Health of Polytechnic Institute of Setubal, Setubal, Portugal

<sup>2</sup>Gynecology / Obstetrics, Amamentos Clinic, Lisbon, Portugal

<sup>3</sup>Ginecologia / Obstetricia, Hospital da Luz, Lisboa, Portugal

**Problem statement:** Infertility is defined as the inability of a couple to conceive or to carry out a pregnancy after, at least, 1 year of unprotected sexual intercourse. Couples with fertility problems often seek acupuncture as a way to optimize clinical outcomes and achieve the goal of pregnancy / take home baby. If evidence is found on the benefits of acupuncture on female fertility, being a safe therapy with few side effects, acupuncture may be considered as a complementary therapeutic technique for the treatment of female fertility problems. The objective is to carry out a literature review, published in the last 5 years, on the impact of acupuncture as a complementary therapy in the treatment of female fertility problems. **Methods:** The database used was Pubmed-Mesh, and the search was performed using the following keywords with the following search strategy: "Infertility" [Mesh] AND "Infertility, Female" [Mesh] AND ("Acupuncture" [Mesh] OR "Acupuncture Therapy" [Mesh]). **Results:** A total of 52 articles were found and literature analysis and synthesis were performed. **Conclusions:** In recent years there has been an increase in the number of published articles about the role of acupuncture in female fertility, which may reflect the growing interest of using acupuncture as a complementary approach in the treatment of female fertility problems. The increase in studies in this area may also contribute to a better understanding of its mechanisms of action and add more evidence to substantiate this complementary therapeutic approach. Acupuncture may constitute a valid complementary therapeutic approach in the treatment of female fertility problems; however, it may be necessary to conduct more high-quality clinical trials.

## NOVEL METHODOLOGY OF SPERM SELECTION: A LOGIC CENTRIFUGATION-FREE ALTERNATIVE TO MICROFLUIDICS

Yolanda Cabello<sup>1,2</sup>, Pedro Belchin<sup>1</sup>, Javier Guerrero<sup>2</sup>, Daniel Ordóñez<sup>1</sup>, Fernandez-Lopez Carmen<sup>3</sup>, Gosalvez Jaime<sup>3</sup>

<sup>1</sup>Embriology, Hospital Ruber Juan Bravo Quironsalud, Madrid, Spain

<sup>2</sup>Embriology, Overture Life, Madrid, Spain

<sup>3</sup>Biology, Universidad Autonoma de Madrid, Madrid, Spain

**Problem statement:** Using sperm in in vitro conditions for Assisted Reproductive Technologies (ART), produces a level of imperative iatrogenic sperm damage affecting most vital structures of the spermatozoa. The use of sperm centrifugation is one of the most para-biological and aggressive interventions that is commonly used in ART. Subsequently, any strategy to avoid its use will reduce the negative impact of iatrogenic sperm damage. Recently, the use of microfluidic based devices has been marketed to avoid centrifugation and subsequently improving the relative quality of the sperm sample that will be used for fertilization. The aim of the present study was to compare the efficiency of sperm selection of microfluidic devices and a new methodology Sperm Selection Centrifugation Free (SSCF). **Methods:** Ten different samples were processed in parallel using a microfluidic device (Fertile chip®, prepared following the manufacturer instructions) and SSCF. The SSCF is a combination of classic sperm swim-up with the use of density gradient reagents. The SSCF creates a layer of mixed sperm with the lower layer gradient reagent (Isolate®, Irvine) 1:1 deposited on the bottom of a conic tube, then covered by the upper layer gradient

reagent (Isolate®, Irvine) and finally, covered with fresh sperm media (Washing®, Irvine). Sperm are left to swim up for 1 minute at room temperature and the top layer recovered for ICSI. After both treatments, samples were assessed for sperm concentration, sperm motility and sperm DNA fragmentation (SDF). **Results:** Sperm concentration: Microfluidics: lower than 0.1 M/ml or failed when the sperm concentration was lower than 12 M. SSCF: 5 M to 30 million per ml. Sperm always recovered. Sperm motility: Microfluidics: Higher than 90% (mean 98%). SSCF: Range 85-45 % (mean 70.9; SD 13.3). Sperm DNA Fragmentation: Microfluidics: 9.2%. SSCF: 10.3% **Conclusion:** The SSCF is a low-cost and efficient alternative to microfluidic devices. Sperm concentration is 100 times higher; sperm motility is slightly lower within the normal range and SDF is clearly reduced without significant differences from microfluidics. The SSCF methodology could be used for ICSI and, unlike microfluidics, in IVF or intrauterine insemination due to a higher concentration of recovered sperm.

## MULTIVARIATE MODELS FOR ASSESSING SUCCESS IN IN VITRO FERTILIZATION. SYSTEMATIC REVIEW AND META-ANALYSIS OF PREDICTIVE FACTORS INFLUENCING RESULTS

Maria Carrera<sup>1</sup>, Carmen Segura<sup>2</sup>, Miguel Caballero<sup>3</sup>, Jose Maria Gris<sup>4</sup>, Federico Perez Milan<sup>3</sup>, Jose Antonio Dominguez<sup>5</sup>

<sup>1</sup>Ginecologia y Obstetricia, Hospital Universitario Doce de Octubre, Madrid, Spain

<sup>2</sup>Unidad de Reproduccion, UR Moncloa, Madrid, Spain

<sup>3</sup>Ginecologia Y Obstetricia, Hospital General Universitario Gregorio Marañon, Madrid, Spain

<sup>4</sup>Ginecologia Y Obstetricia, Hospital Universitario Vall d'Hebron, Barcelona, Spain

<sup>5</sup>Unidad De Reproduccion, IERA, Badajoz, Spain

### Problem:

IVF treatments are complex and expensive so infertile couples should be accurately informed about chances of success to manage expectations and make decisions. Prediction models can help clinicians counsel patients. **Methods:** Systematic review of multivariable predictive models of pregnancy or life birth in IVF with meta-analysis of main predictive factors. Following databases were searched: MEDLINE, PubMed, Embase, Web of Science, Cochrane Library, Google Scholar, clinicaltrials.gov, EudraCT. **Inclusion criteria:** Studies developing multivariate predictive models in IVF with fresh embryo transfer reporting unadjusted Odds Ratios (OR) of predictors suitable for pooled analysis. **Exclusion criteria:** Predictive models in other ART. Model validation studies. Outcome was pregnancy or life birth. Eligibility was addressed using CHARMS checklist. Selection process was documented by a PRISMA flow chart. Quality of included studies was assessed using TRIPOD checklist, and risk of bias was appraised using PROBAST checklist. Revman 5.3 has been used for data analysis with random effects model. Heterogeneity was measured using Higgins I<sup>2</sup>. Protocol was registered in PROSPERO number: CRD42020185229. **Results:** 3195 records were identified, 1968 left after duplicates and 117 assessed for eligibility. 26 studies were included in the qualitative synthesis and 21 predictive models in the meta-analysis: Stolwijk, 1996, Syrop, 1999, Bancsi, 2000, Strandell, 2000, Hart, 2001, Maugey-Laulom, 2002, Sharma, 2002, Hunault, 2002, Ferlitsch, 2004, Hauzman, 2004, Ottosen, 2007, Sabatini, 2008, Van Weert, 2008, Wang, 2008, Lien, 2010, Nelson, 2011, Cai, 2011, Dhillon, 2016, Huang, 2018, Xu, 2019 and Zhang, 2019. 15 predictive factors have been meta-analysed. Those with a significant pooled OR have been: Age: OR 0.94 (0.92-0.95) N=12 studies; Infertility length: OR 0.97 (0.95-0.99) N=5; Endometriosis as IVF indication: OR 0.70 (0.63-0.76) N=2; basal FSH: OR 0.95 (0.91-0.99) N=5; Antral Follicle Count (AFC): OR 1.02 (1.01-1.02) N=3;

Oocytes recovered: OR1.04 (1.02-1.06) N=5, total number of embryos: OR=1.10 (1.06-1.13), N=2 and transfer of 2 vs 1 embryo: OR=2.88 (1.98-4.20) N=2. **Conclusions:** Predicting chances of success in IVF help adequate treatment and manage expectations. Patient age, infertility length, endometriosis diagnosis, ovarian reserve markers, n° of oocytes and embryos obtained and transferred embryos are factors significantly associated with success.

#### DIAGNOSTIC ACCURACY OF SUBMUCOSAL FIBROIDS IN INFERTILE WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS

Jose Maria Gris<sup>1</sup>, Maria Carrera<sup>2</sup>, Carmen Segura<sup>3</sup>, Miguel Caballero<sup>4</sup>, Federico Perez Milan<sup>4</sup>, Jose Antonio Dominguez<sup>5</sup>

<sup>1</sup>Ginecología Y Obstetricia, Hospital Universitario Vall d'Hebron, Barcelona, Spain

<sup>2</sup>Ginecología Y Obstetricia, Hospital Universitario Doce de Octubre, Madrid, Spain

<sup>3</sup>Unidad De Reproduccion, UR Moncloa, Madrid, Spain

<sup>4</sup>Ginecología Y Obstetricia, Hospital General Universitario Gregorio Marañon, Madrid, Spain

<sup>5</sup>Unidad de Reproduccion, IERA, Badajoz, Spain

**Problem statement:** Histology, as former gold standard in submucosal fibroids diagnosis, has been gradually displaced by hysteroscopy. But due to invasiveness and need of expertise, easier and universally available techniques as 2D and 3D ultrasound and 2D and 3D sonohysterography might be useful in intracavitary fibroids diagnosis in infertile women. **Methods:** Systematic review and meta-analysis of diagnostic studies comparing 2D and 3D ultrasound and sonohysterography accuracy with hysteroscopy and histology has been performed following PRISMA guidelines. The following databases have been searched: MEDLINE, PubMed, Embase, Web of Science, Cochrane Library and Google Scholar. Selection process has been documented by a PRISMA flow chart. Quality assessment of included studies was performed using STARD and QUADAS-2 tool. Meta-analysis has been performed with Meta-DiSk and pooled sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratios, and diagnostic Odds Ratio (DOR) have been calculated. **Results:** 1190 records have been identified after removal of duplicates and 49 have been included in the qualitative synthesis and 22 in the meta-analysis. When comparing 2D ultrasound with hysteroscopy (N=7), pooled DOR has been 532,5 (95%CI 185,83 to 1525,8). Area under ROC curve (AUROC) has been 0,9904 (95%CI 0,98 to 0,9994). When comparing 2D ultrasound with histology (N=6), pooled DOR has been 62,997 (95% CI 12,422 to 319,49). AUROC has been 0,924 (95% CI 0,826 to 1,02). When comparing 2D sonohysterography with hysteroscopy (N=9), pooled DOR has been 372,13 (95% CI 93,75 to 1477). AUROC has been 0,988 (95% CI 0,966 to 1,009). When comparing 3D sonohysterography with hysteroscopy (N=3), pooled DOR has been 2021,9 (95% CI 342,11 to 11949,1). AUROC has been 0,995 (95% CI 0,99 to 1,002). When comparing sonohysterography with histology (N=7), pooled DOR has been 231,05 (95% CI 78,564 to 679,5). AUROC has been 0,986 (95% CI 0,965 to 1,007). **Conclusion:** Despite hysteroscopy can be considered the gold standard for intracavitary lesions diagnosis, both 3D and sonohysterography showed good accuracy and are non-invasive and universally applicable techniques.

#### CONSTRUCTION AND VALIDATION OF A MULTIVARIATE PREDICTIVE MODEL OF TWIN PREGNANCIES AFTER DAY 3 FRESH DOUBLE EMBRYO TRANSFERS

Maria Carrera, Laura Marqueta, Laura de la Fuente, Elisa Escalante, Nerea Ruiz, Pilar Moreno  
Unidad De Reproduccion, Hospital Universitario Doce De Octubre, Madrid, Spain

**Problem statement:** Despite available techniques for embryo selection for single embryo transfer, still 65.1% of transfers in Europe are of  $\geq 2$  embryos (ESHRE,2014), which has led to a twin pregnancy rate of 17%. Our aim is to develop and validate a multivariate prediction model of twin pregnancy with a risk score that helps in daily clinical decision making selecting suitable patients for day 3 single embryo transfer maintaining pregnancy rates. **Methods:** Retrospective cohort study of 830 IVF-ICSI cycles with ongoing pregnancy after double embryo transfer DET performed in a Spanish Public IVF program in 2009-2018. Model was adjusted using backward-stepping logistic regression by maximum likelihood ratio. Goodness of fit was assessed with Hosmer-Lemeshow test. Model discriminatory power was assessed with AUROC. External validation was performed in a retrospective cohort of 757 IVF-ICSI cycles after DET from another Spanish Public IVF program of similar characteristics in 2009-2018. Statistical analysis was carried out using SPSS20.0 and Stata14.0. For both developing and validating models TRIPOD checking list was used. **Results:** Twin pregnancy rate was 26.9%. Two risk models for twin pregnancies were developed based on age; one for patients  $\leq 37$  (TwinR-Score-36) and another for patients from 37-40 (TwinR-Score-37). For patients  $\leq 37$ , six independent factors were found: BMI30, IVF cycle number, Ovarian Sensitivity Index 250 (defined by Biasoni as mature oocytes/total FSHIU), having one grade A embryo (ALPHA classification), not having grade D embryos and having more than four embryos available. Goodness of fit was good,  $X^2=2.7(p=0.44)$ , but discriminatory power was low, AUROC=0.61(0.56-0.66). For patients  $\geq 37$ , apart from the six previous factors, having and infertility 12 months was also an independent risk factor. Goodness of fit was good,  $X^2=1.16(p=0.76)$ , with low discriminatory power AUROC=0.64(0.54-0.75). Two risk scores were developed based on Twin-R-Score 36 and 37. In the validation cohort, both discriminatory power and goodness of fit were similar to the construction cohort. **Conclusions:** Main weakness is low predictive power. Small sample size and retrospective design may have contributed. As external validation has shown similar predictive power, Twin-R-Scores might be useful tools in clinical decision making for enhancing single embryo transfer.

#### POSITIVE ASSOCIATION OF POLYMORPHISM IN CYP19A1 GENE WITH FEMALE INFERTILITY SUSCEPTIBILITY

Maria Manuel Casteleiro Alves<sup>1,2</sup>, Micaela Almeida<sup>1</sup>, Antonio Helio Olini<sup>2,3</sup>, Luiza Breitenfeld<sup>1</sup>, Ana Cristina Ramalhinho<sup>1,2</sup>

<sup>1</sup>Health Sciences Research Centre (CICS), Faculty of Health Sciences, University of Beira Interior (UBI), Covilha, Portugal

<sup>2</sup>Assisted Reproduction Laboratory, Academic Hospital of Cova da Beira (CHUCB), Covilha, Portugal

<sup>3</sup>Sao Jose do Rio Preto School of Medicine (FAMERP), Gynaecology and Obstetrics, Sao Jose do Rio Preto, Brazil

Aromatase catalyzes the final step in biosynthesis of estrogens and is encoded by the gene CYP19A1. The CYP19A1 gene is located on chromosome 15q21.1. It is a member of the cytochrome P450 superfamily which are mono-oxygenases that catalyze many reactions involved in steroidogenesis. The Trp/Arg polymorphism at codon 39 of the CYP19A1 (W39R) results in three genotypes TT, TC and CC. This polymorphism has been associated with a change of aromatase activity that affects estrogens levels, which can lead to the development of various diseases. This case-control study was conducted in order to evaluate the potential role of CYP19A1 in modulating individual susceptibility to female infertility. Case subjects, 201 women with infertility were enrolled between October 2015 and July 2019. 161 fertile female controls, with no previous history of infertility, no previous history of gynecological

pathologies compatible with infertility, and no previous history of IVF treatments, were selected in Obstetrics Consultation. Blood was collected by venous puncture as part of the routine analyses. Genomic DNA was extracted. Genotyping for CYP19A1 was performed by polymerase chain reaction-based methods with confronting two-pair primers. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated by unconditional logistic regression. We obtained the following genotypes distribution for the study group (n=201): TT-52; TC-145 and CC-4. For the control group (n=161) we obtained the following genotypes distribution: TT-96; TC- 65 and CC-0. By the analysis of the results it seems that there is a higher prevalence of TC/CC genotype carriers with infertility causes such as: endometriosis risk (OR 4.554; 95% CI 2.209-9.386; p<0.001); polycystic ovary syndrome (PCOS) risk (OR 5.317; 95% CI 2.767-10.215; p<0.001); premature ovarian failure (POF) (OR 3.376; 95% CI 1.672-6.815; p<0.001) and tubal pathology (OR 3.231; 95% CI 1.653-6.314; p<0.001). Finally, a strong association of TC/CC genotype with female infertility, regardless of the cause, was found (OR 4.232; 95% CI 2.710-6.609; p<0.001). In conclusion, women carriers of TC/CC genotype in CYP19A1 gene, seem to present increased susceptibility to infertility. **Keywords:** Aromatase; CYP19A1; Polymorphisms; Infertility

#### IN VITRO FECUNDATION AS SECOND OPTION FOR COUPLES DIAGNOSED WITH UNEXPLAINED INFERTILITY

Caterina Ceccarelli, **Alejandra Santana Suarez**, Carla Mendoza Rodriguez, Marta Armas Roca, Lourdes Roldan Gutierrez, Nelda Benitez Castillo, Monica Alvarez Sanchez, Jose Tabares Concepcion  
Unidad de Reproduccion Humana, Complejo Hospitalario Universitario Insular Materno Infantil, Las Palmas de Gran Canaria, Spain

**Problem statement:** Historically, a gradual progression in treatment of couples diagnosed with Unexplained Infertility has been proposed, starting with the least invasive and least expensive option. The trend is to offer In Vitro Fertilization (IVF) to couples who have already had three cycles of artificial insemination without success. The objective of the study is to know the gestation rate achieved in IVF cycles after failure with IAC. **Methods:** Retrospective, observational study carried out between 2008 and 2019 including all IVF cycles performed in couples with Unexplained Infertility, with nulligravid women under 35 years of age. The results were analyzed according to the gestation rate. **Results:** 148 IVF cycles were performed. The mean age was 32.19 years (24.35-35.03). The pregnancy rate per cycle was 44.8% and the accumulated rate was 62.9%. There were statistically significant differences in the dose of Follicle-Stimulating Hormone (FSH) (2035.19 IU vs 1520.41 IU, p 0.05) and Human Menopausal Gonadotropin (HMG) (1021.08 IU vs 581.25 IU, p 0.05) prescribed as well as the number of fresh embryos transferred (1.98 vs 1.42, p 0.000), being higher in the group of patients who achieved pregnancy. The type of stimulation and the type of fertilization were not statistically significant. In the group with a positive pregnancy rate, there were more embryo vitrifications (p 0.05), these patients being younger and thinner. **Conclusion:** IVF is the treatment that provides both the best clinical information and effectiveness. In young couples with Unexplained Infertility it is an option that provides very good results and it could be considered as the first therapeutic strategy.

#### PERINATAL RESULTS IN IN VITRO FECUNDATION CYCLES FOR UNEXPLAINED INFERTILITY

Caterina Ceccarelli, **Alejandra Santana Suarez**, Carla Mendoza Rodriguez, Monica Alvarez Sanchez, Lourdes

Roldan Gutierrez, Nelda Benitez Castillo, Marta Armas Roca, Jose Tabares Concepcion  
Unidad De Reproduccion Humana, Complejo Hospitalario Universitario Insular Materno Infantil, Las Palmas De Gran Canaria, Spain

**Problem statement:** The diagnosis of reproductive dysfunction of unknown origin is made when bilateral tubal patency, normal ovulatory function and normal seminogram are tested after one year of infertility. The objective of the study is to know the perinatal results in IVF cycles of couples with Unexplained Infertility. **Methods:** Retrospective case-control study carried out between 2008 and 2019 including all IVF cycles performed after failure of the IAC in couples with Unexplained Infertility, with nulligravid women under 35 years of age. Perinatal outcomes were analyzed and compared with a cohort of non-sterile patients. **Results:** 148 IVF cycles were performed with a cumulative gestation rate of 62.9%: 67.7% were single gestations, 29.2% twin and 3.1% triple. Of the 65 pregnancies archived, 58 reached term, 5 were abortions, 1 ectopic pregnancy and 1 antepartum fetal death. We compared the perinatal outcomes of single pregnancies with a cohort of 132 healthy patients with the same demographic characteristics. No statistically significant differences were obtained in maternal or gestational pathology (p = 0.900 and p = 0.350, respectively). Concerning the delivery 54.5% were induced and 12.1% underwent a planned cesarean section (vs 38.2% and 0%, respectively, p 0.000). Of the patients who started labor, 27.3% ended in cesarean section (vs 6.9%, p 0.05). There were no differences regarding perinatal outcomes. **Conclusion:** The perinatal results in patients undergoing IVF with a diagnosis of Unexplained Infertility do not differ from the general population, but there is a higher percentage of deliveries by cesarean section.

#### MISCARRIAGE RATE AFTER ASSISTED REPRODUCTIVE TECHNOLOGIES

Ines Lourenco<sup>2</sup>, Madalena Tavares<sup>3</sup>, Joaquim Nunes<sup>1</sup>, Ana Aguiar<sup>1</sup>, Sandra Sousa<sup>1</sup>, Isabel Pereira<sup>1</sup>, Fernanda Leal<sup>1</sup>, Marta Carvalho<sup>1</sup>, Carlos Calhaz-Jorge<sup>1</sup>

<sup>1</sup>Departamento de Obstetricia, Ginecologia e Medicina da Reproducao, Centro Hospitalar Lisboa Norte - Hospital de Santa Maria, Lisbon, Portugal

<sup>2</sup>Departamento de Ginecologia e Obstetricia, Hospital Beatriz Angelo, Loures, Portugal

<sup>3</sup>Ginecologia e Obstetricia, Hospital de Vila Franca de Xira, Vila Franca de Xira, Portugal

**Problem Statement:** In vitro fertilization (IVF) and Intracytoplasmic sperm injections (ICSI) are associated with an increased risk of adverse obstetric and perinatal outcomes, even in single pregnancies. Early pregnancy loss is not a rare complication in general and occurs in 5 to 15% of all pregnancies. According to literature the rate of early pregnancy loss in post-IVF/ICSI pregnancies is higher than 15%. Our aim was to determine the rate of spontaneous miscarriage rate loss after fresh embryo transfer in IVF/ICSI cycle and identify characteristics of the population that may be associated with this outcome. **Methods:** Data of all IVF or ICSI cycles resulting in pregnancy after fresh embryo transfer in our institution from January 2009 until December 2018 were retrospective reviewed. Ectopic pregnancies, medical pregnancy terminations and late miscarriages were excluded from the study. We divided our sample in two groups: Spontaneous first trimester miscarriage (Group 1) and evolutive pregnancies (Group 2). We studied and compared both groups according to demographic, clinical and IVF/ICSI cycle characteristics. Data were analyzed using SPSS® software with application of X2 and Mann-Whitney U tests. **Results:** From the 1122 included cases, there were 192 early pregnancy losses and 930 live births. The rate of early pregnancy loss was 17.1%. Differences between groups 1

and 2 were statistically significant ( $p < 0.05$ ) regarding mean age (higher for Group 1) and number of embryos transferred (lower for Group 1). The spontaneous early miscarriage rate was 6.8% in multiple pregnancies and 21.2% in single pregnancies. **Conclusion:** In our population, spontaneous first trimester miscarriage rate was superior to those reported for the general population and similar to the rate described by other authors regarding pregnancy after IVF/ ICSI techniques. Advanced maternal age and a lower number of embryos transferred seems to be associated with a higher likelihood of an early pregnancy loss.



Young Scientist Abstract

### PREIMPLANTATION EMBRYONIC MOSAICISM AND MATERNAL AGE IN INVITRO FERTILIZATION CYCLES

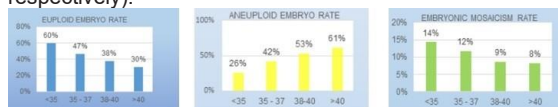
Maria Jose Mendiola<sup>1</sup>, Jazmin Meza<sup>2</sup>, Fiorella Castillo<sup>1</sup>, Julio Huayhua<sup>3</sup>, Naomi Inoue<sup>2</sup>, Luis Noriega-Hoces<sup>1</sup>, Luis Guzman<sup>1,3</sup>

<sup>1</sup>Lima, Clínica Concebir, Lima, Peru

<sup>2</sup>Grupo de Reproducción Asistida, PRANOR Laboratorio, Lima, Peru

<sup>3</sup>Lima, ADN diagnóstico, Lima, Peru

**Problem statement:** Preimplantation genetic testing for aneuploidies (PGT-A) is a technique used in IVF procedures to identify euploid embryos prior to transfer decreasing the frequency of spontaneous abortions. Advanced maternal age has demonstrated to increase aneuploidies. However, there is discrepant information about the impact of maternal age on the frequency of embryonic mosaicism. **Methods:** This non-randomized prospective study included 1887 IVF cycles with PGT-A analysis from January 2016 to January 2020, divided into four groups stratified by maternal age (using the SART classification): group 1 (under 35 years), group 2 (35 to 37 years old), group 3 (38 to 40 years old), and group 4 (over 40 years old). **Results:** The rate of euploid embryos was significantly higher in patients of group 1 compared to groups 2 3 and 4 (60%, 47%, 38% and 30%, respectively  $p < 0.001$ ). Additionally, the aneuploid embryo rate was significantly higher in group 4 (61%) compared to group 1 (26%) and 2 (42%). Regarding embryonic mosaicism, the rate was significantly higher in patients of group 1 compared to groups 2 3 and 4 (14%, 12%, 9% and 8%, respectively).



**Conclusion:** Our findings suggest that the rate of embryonic mosaicism is higher in patients younger than 35 years. The aneuploidy rate increases with maternal age. It is necessary to assess the clinical utility of preimplantation genetic tests in patients younger than 35 years. *The Authors declare that there is no conflict of interest.*

### ARTIFICIAL INSEMINATION AS FIRST CHOICE IN COUPLES WITH UNEXPLAINED INFERTILITY

Carla Mendoza Rodriguez, Alejandra Santana Suarez, Lourdes Roldan Gutierrez, Monica Alvarez Sanchez, Marta Armas Roca, Nelda Benitez Castillo, Jose Tabares Concepcion, Caterina Ceccarelli

Unidad De Reproducción Humana, HUMIC, Las Palmas, Spain

**Introduction:** The diagnosis of unexplained reproductive dysfunction is made when bilateral tubal patency, normal ovulatory function and normal semen analysis are verified after one year of infertility. The proportion of couples with unexplained infertility is approximately 16%. Currently, there is no consensus on what the first line of treatment should be in this type of patient: expectant attitude, artificial

insemination (AI) or in vitro fertilization. Thus, in most cases, management is typically empirical, taking into account the efficacy, safety, cost, and risks of each treatment option. The objective of the study is to know the gestation rate of artificial inseminations in couples with a diagnosis of idiopathic sterility and a good reproductive prognosis. **Methods:** Retrospective observational study carried out between 2008 and 2019 in which all the AIs carried out in couples with a diagnosis of unexplained infertility, nulliparous and women under 35 years were included. **Results:** A total of 8174 first visits were attended, of which 1162 met unexplained infertility criteria (13.6%). A total of 806 AIs were performed in 329 couples. The mean age was 31.63 years (23.36-35.10) and the mean sterility time was 2.53 years (1-10). The gestation rate per cycle was 13% and the cumulative rate was 30.6%, showing a statistically significant decrease in pregnancy rates after the third insemination ( $p < 0.000$ ).

**Conclusion:** It seems reasonable to start with an empirical management of this group of patients, achieving good cumulative pregnancy rates in the first three insemination cycles.

### PREDICTORS OF SUCCESS FOR ARTIFICIAL INSEMINATIONS IN COUPLES WITH UNEXPLAINED STERILITY

Carla Mendoza Rodriguez, Alejandra Santana Suarez, Lourdes Roldan Gutierrez, Monica Alvarez Sanchez, Marta Armas Roca, Nelda Benitez Castillo, Jose Tabares Concepcion, Caterina Ceccarelli

Unidad De Reproducción Humana, HUMIC, Las Palmas, Spain

**Introduction:** The diagnosis of unexplained infertility is made when all the diagnostic tests that we have are normal and the couple has been having regular unprotected sex for a year. That is why, even today, there is no consensus on what the first line of treatment in this type of patient should be: expectant attitude, artificial insemination (AI) or in vitro fertilization (IVF). The study's objective is to determine possible predictors of poor prognosis of AI in this type of couples. **Methods:** Retrospective observational study carried out between 2008 and 2019 in which all the AIs performed in couples with unexplained infertility diagnosis, nulliparous and women under 35 years were included. The results were analyzed according to the gestation rate. **Results:** A total of 806 AIs were performed in 329 couples with idiopathic sterility. There were no statistically significant differences between patient's characteristics (age, BMI and time of infertility) or in seminal parameters or ovarian stimulation between those couples who achieved pregnancy versus those who did not. **Conclusions:** In general terms, the prognosis will depend fundamentally on age

### LIVE BIRTH RATES AFTER ASSISTED REPRODUCTIVE TECHNIQUES OF ADVANCED AGED WOMEN

Gulnaz Sahin, Ege Nazan Tavmergen Goker, Ferruh Acet, Erol Tavmergen

Family Planning and Infertility Research and Practice Center, Ege University, Izmir, Turkey

**Problem Statement:** Declining number and quality of oocytes by advancing female age is a well-known phenomenon. The success of assisted reproductive techniques (ART) is strictly dependent on the female age. Fertility treatment in women aged after the forty's remains difficult and controversial. The evaluation of the chance of a live birth with their own gametes in an ART program is important to appropriately counsel these patients. Our aim was to analyze ART outcomes of women at extremely advanced age in our tertiary IVF center. **Methods:** A total of 178 women who underwent oocyte retrieval and subsequent fresh and/or frozen-thawed autologous embryo

transfer (ET) between 2015-2020 years, were retrospectively analyzed. Female age 42 years during the oocyte retrieval was the inclusion criteria for this study. ICSI and assisted hatching was used for all included cycles. The main outcome measures were live birth (LB) and clinical pregnancy rates (CPR) of these patients. **Results:** Totally 261 opu cycles were performed in 178 women aged over 42. The mean age was 44.5 (SD:1.4, min: 43-max:49). Male factor (16.8%) and tubo-peritoneal factor (%1.1) were concomitant factors. Of those 261 cycles; 137 ended up with fresh ET, 87 cycles there were no embryos available for transfer and remaining 37 cycles embryos were cryopreserved. Subsequent 16 frozen-thawed ET cycles were performed in 16 women. Finally, 118 women (66.3%) underwent either autologous fresh or frozen ET cycles (n=153) and 60 women (33.7%) could not reach ET. Twelve pregnancies were obtained (biochemical=3, miscarriage=7 and live birth=2). Clinical pregnancy and LBR's were (5.0%, 1.1% per patient), (5.8%, 1.3% per ET) and (3.4%, 0.7% per cycle), respectively. Those patients who had live birth both were 43 years old at oocyte retrieval and their pregnancies were obtained from frozen thawed ET. **Conclusion:** The pregnancy and live birth rates are extremely low for those patients at very advanced age, however there might be extreme cases with successful result. Availability of supernumerary embryos for future frozen-thawed transfers might give a chance these patients to conceive. As with all infertile patients, an individualized approach should be taken into account in advanced age groups.

#### OIL EQUILIBRATION TIME HAS AN IMPORTANT IMPACT ON BLASTOCYST DEVELOPMENT

**Marta Sanchez De Burgos,** Pedro Belchin Fernandez, Elena Izquierdo Trechera, Alberto Garcia Enguidanos, Daniel Ordóñez, Perez Embryology, Hospital Universitario Ruber Juan Bravo, RUBERFIV, Madrid, Spain

**Introduction:** To obtain an increase in useful blastocyst rate is a goal in all assisted reproduction clinics. Having more blastocyst we can improve the selection of the embryos and therefore have more chances to achieve a pregnancy. Culture conditions have a strong effect on the development of the embryos and particularly on the blastocyst formation. One of the parameters that have been checked along the time is the oil and the time that is required in order to ensure a correct pH of the culture media. **Objective:** To investigate if extended oil equilibration time has an impact on embryo development rate in patients undergoing IVF. **Design:** Observational and retrospective study. **Materials and methods:** A total of 92 embryos obtained from 22 egg donor cycles were included in the study. All the patients underwent an IVF cycle at Hospital Universitario RUBER Juan Bravo, RUBERFIV from January 2019 to June 2020. ICSI was performed in all cycles in order to inseminate the oocytes. Exclusion criteria were the following: altered karyotype, single gene disorder and male factor. Embryo morphology was checked at cleavage state and blastocyst state (day 5 or 6). The embryo with the highest morphology grade was selected for embryo transfer; all not transferred embryos that reached blastocyst state (grade 3 or higher, Gardner Score) were vitrified. Embryos were divided in two groups based on the oil equilibration time: 4 hours (control group) and overnight (study group). Main outcome was the useful blastocyst rate (transferred and vitrified blastocyst) observed in the different groups. Other parameters analysed were sperm concentration, sperm motility. Chi square was used for categorical variables.

		overnight
MII	109	101
Zygotes	90	77
Useful Blastocyst Rate (n)	47 % (43)	63 % (49)

**Results:** Descriptive parameters showed no differences in sperm concentration or sperm motility. Statistical model showed significant differences among groups ( $p=0.0385$ ). **Conclusion:** Increased blastocyst rate is associated with extended oil equilibration time. A further analysis with higher size and other parameters that can be involved currently undergoing.



Young Scientist Abstract

#### IS MORE, BETTER? PREDICTING THE LIKEHOOD OF LIVE BIRTH ACCORDING TO THE NUMBER OF OOCYTES RETRIEVED AFTER OVARIAN STIMULATION FOR IN VITRO FERTILIZATION

**Marina Sousa Gomes**<sup>1</sup>, Sara Nunes<sup>2</sup>, Daniela Sousa<sup>3</sup>, Raquel Brandao<sup>3</sup>, Emidio Vale Fernandes<sup>3</sup>, Claudia Lourenco<sup>3</sup>, Isabel Sousa Pereira<sup>3</sup>, Carla Leal<sup>3</sup>, Marcia Barreiro<sup>3</sup>

<sup>1</sup>Obstetrics and Gynecology, Alto Minho Local Healthcare Unit, Viana do Castelo, Portugal

<sup>2</sup>Obstetrics and Gynecology, Hospital Center of Tras-os-Montes and Alto Douro, Vila Real, Portugal

<sup>3</sup>Centre of Assisted Medical Procreation, Maternal Child Centre of the North, Porto, Portugal

**Problem statement:** Numerous studies about the number of retrieved oocytes and pregnancy outcomes have been published with controversial results. The objective of this study was to evaluate the impact of the number of retrieved oocytes after ovarian stimulation for in vitro fertilization on cumulative live birth rates (CLBRs). **Methods:** We retrospectively examined the cycles of 1282 women undergoing in vitro fertilization therapy at Centro Materno-Infantil do Norte (Porto, Portugal) from January 2011 to March 2019. Patients were categorized into five groups according to the number of oocytes retrieved: 1–3 oocytes, 4–9 oocytes, 10–14 oocytes, 15–24 oocytes, and 25 oocytes and above. The primary outcome was the CLBR defined as the delivery of a live-born infant (24 weeks of gestation) in the fresh or in the subsequent frozen-thawed cycles in relation to the number of oocytes retrieved. The secondary outcome was live birth after the fresh cycle. **Results:** The median number of oocytes retrieved was 9 (interquartile range, 6–14) and the median age of patients was 36 (interquartile range, 33–38). The overall CLBR was 23.4%. The results from the multivariable regression analysis showed that the number of oocytes retrieved remained a significant predictor (AOR 1.033; CI 1.010–1.055;  $p=0.004$ ) of CLBR after adjusting for female age, and BMI. CLBR steadily increased with the number of oocytes retrieved: 1–3 oocytes, 13.5%; 4–9 oocytes, 16.3%; 10–14 oocytes, 27.7%; 15–24 oocytes, 36.4%; and 36.4% with more than 25 oocytes. Regarding the fresh cycle outcome, live birth remained relatively unchanged between 10 and 24 oocytes retrieved. A drop in fresh live birth rates was identified thereafter, with a progressive increase in the “freeze-all” cycle rate. **Conclusion:** The current study demonstrates that CLBRs continuously increase with the number of oocytes retrieved, suggesting that ovarian stimulation may have a very minimal or no detrimental effect on oocyte/embryo quality.



Young Scientist Abstract

## PRESERVATION OF PRIMORDIAL FOLLICLE RESERVE BY PHARMACOLOGICAL INHIBITORS TARGETING THE PI3K/PTEN/AKT, MTOR AND JNK PATHWAYS IN MURINE OVARIAN CULTURE

Carmen Terren<sup>1</sup>, Michelle Nisolle<sup>1,2</sup>, Carine Munaut<sup>1</sup>

<sup>1</sup>Laboratory of Tumor and Development Biology, GIGA-Cancer, University of Liege, Liege, Belgium

<sup>2</sup>Department of Obstetrics and Gynecology, Hopital de la Citadelle - University of Liege, Liege, Belgium

**Problem statement:** Cryopreservation of ovarian tissue containing immature primordial follicles followed by auto-transplantation (OTCTP) is the only option available to preserve the fertility of prepubertal patients or patients requiring urgent therapy for aggressive malignancies. However, a major obstacle in this process is follicular loss immediately after grafting, possibly due to slow neovascularization, apoptosis and/or massive follicular recruitment. Our aim was to test inhibitors of primordial follicle activation in whole ovaries organotypic in vitro culture to preserve the primordial follicle pool. **Methods:** Activation of PI3K/PTEN/Akt, mTOR and JNK signaling pathways in 4-8-weeks old murine ovaries cultured on transwell membrane inserts with/without inhibitors (LY294002, a powerful PI3K inhibitor; rapamycin, the specific mTOR inhibitor or SP600125, a JNK pathway inhibitor) were determined by Western Blot and immunofluorescence analyses. Follicles were quantified according to their maturation degree on histological sections. **Results:** PI3K/PTEN/Akt, mTOR and JNK signaling pathways were activated by cryopreservation. A 24h organotypic culture of whole ovaries induced the activation PI3K/PTEN/Akt and mTOR signaling pathways and a decrease of the JNK pathway. Addition of different inhibitors such as LY294002 and SP600125 reduced the activation of the PI3K/PTEN/Akt whereas rapamycin reduced the activation of the mTOR pathway. Quantification of follicle density indicated a better preservation of primordial follicles after culture in presence of LY294002 (25µM), rapamycin (1µM) or SP600125 (50µM) as compared to the control condition. Concomitantly, the proportion of growing follicles was decreased with LY294002 and rapamycin for a 2-days culture, indicating inhibition of follicle activation. **Conclusion:** Primordial follicles are activated by cryopreservation and organotypic in vitro culture. Pharmacological inhibition of primordial follicle activation signaling pathways allows to preserve the primordial follicle pool by reducing the activation of the PI3K/PTEN/Akt, mTOR and JNK pathways. This study underscores that in vitro organotypic culture of whole ovaries is a useful model to mimic follicle activation occurring after OTCTP. Moreover, our results indicate that ovarian graft lifespan could be extended through the use of pharmacological inhibitors of PI3K/PTEN/Akt and mTOR pathways.

## IMPROVING MATERNAL HEALTH: DO SINGLETON PREGNANCIES EFFECTIVELY MITIGATE THE MEDICAL, ETHICAL AND LEGAL RISKS ASSOCIATED WITH INVASIVE FERTILITY TREATMENT?

Anna Ulyanenkova<sup>1</sup>, Katherine Drabiak, JD<sup>1,2</sup>

<sup>1</sup>Morsani College of Medicine, USF Health, Tampa, USA

<sup>2</sup>College of Public Health, USF Health, Tampa, USA

**Problem Statement:** While assisted reproductive technologies (ARTs) have become widely available, multiple studies have shown that they are associated with increased maternal morbidities. In Committee Opinion Number 671 (2016), ACOG acknowledges this increased risk, even for singleton pregnancies, and states that it remains unclear if it is due to infertility itself or certain aspects of treatment. Given ART's increased popularity, it

is important to consider whether current guidelines effectively mitigate risks associated with treatment by examining both female and male factor infertility. **Methods:** A review of current research, legal statutes and cases, data from the CDC and SART, and guidelines from ACOG, SART, ASRM, and the AUA was conducted in summer 2019 that examined regulations governing the fertility industry, industry guidelines, and state laws pertaining to insurance coverage for services. **Results:** Though current guidelines recommend an evaluation of the male partner "from the outset," it is estimated that a male evaluation is not performed for up to 27% of infertile couples. Unfortunately, male infertility is considerably overlooked due to limited insurance coverage. To combat this problem, we propose extending coverage for the screening, diagnosis, and treatment for male infertility; which is currently mandated in only 16 states. Additionally, insufficient surveillance and reporting of adverse events prevents both patients and physicians from knowing the true prevalence of associated risks. This places physicians at risk for litigation by overstating potential benefits of treatment. We recommend establishing a defined list of adverse events, utilizing automatic and mandated reporting systems, and ensuring that infertility data is collected equally from both males and females. **Conclusion:** As infertility treatment becomes more widely used, we must assess whether current guidelines are enough to minimize risks to those most vulnerable. We argue that a greater focus on male infertility and improved surveillance and reporting systems could help minimize maternal risk. Since these recommendations would also improve informed consent and increase transparency, they have positive legal and ethical implications for both physicians and patients. **Disclosure of Interest:** This research was supported by a scholarly award from Research, Innovation & Scholarly Endeavors at USF Health, Morsani College of Medicine.

## DOES BODY MASS INDEX EFFECT IN VITRO FERTILISATION OUTCOME IN POLYCYSTIC OVARIAN SYNDROME?

Nur Dokuzeylul Gungor<sup>2</sup>, Arzu Yurci<sup>1</sup>

<sup>1</sup>IVF Clinic, Memorial Kayseri Hospital, Kayseri, Turkey

<sup>2</sup>IVF Clinic, Medicalpark Goztepe Hospital, Istanbul, Turkey

**Problem statement:** Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy which effects 5-15% of women in reproductive age. To investigate the effects of body mass index (BMI) on the outcomes of in vitro fertilization (IVF) in patients with PCOS. **Methods:** This retrospective, cross-sectional study was conducted with 304 women aged 18-40 years who underwent IVF treatment between January 2015 and December 2019. Approval for the study was granted by the Local Institutional Review Board. The patients were divided into three groups according to BMI cut-off points: group 1 (normal weight: 18.5 kg/m<sup>2</sup> ≤ BMI 24.9 kg/m<sup>2</sup>), group 2 (overweight: 25 kg/m<sup>2</sup> ≤ BMI 29.9 kg/m<sup>2</sup>) and group 3 (obese: 30 kg/m<sup>2</sup> ≤ BMI 35 kg/m<sup>2</sup>). The basic characteristics of the PCOS patients, the details of IVF treatment and the pregnancy outcomes were collected. **Results:** There were no significant difference among the normal weight, overweight and obese PCOS patients undergoing IVF on the clinical pregnancy rate, ongoing pregnancy rate and live birth rate (p>0.05). Although overweight and obese PCOS patients required more gonadotropin (p<0.001) as well as longer stimulation period (p<0.001). **Conclusion:** Higher BMI had no negative effects on the outcomes of IVF patients with PCOS. **Key words:** Polycystic ovary syndrome (PCOS), In Vitro Fertilisation (IVF), Body Mass Index (BMI), obesity

## DIAGNOSTIC PROCEDURES

### A RELIABLE METHOD TO ASSESS CERVICAL STIFFNESS, TOWARDS THE PREDICTION OF PRETERM BIRTH

Sabrina Badir<sup>1</sup>, Laura Bernardi<sup>1</sup>, Francisco Feijo Delgado<sup>1</sup>, Katharina Quack Loetscher<sup>2</sup>, Gundula Heibisch<sup>3</sup>, Irene Hoesli<sup>4</sup>

<sup>1</sup>Pregnotia AG, Pregnotia AG, Schlieren, Switzerland

<sup>2</sup>Clinic of Obstetrics, University Hospital Zurich, Zurich, Switzerland

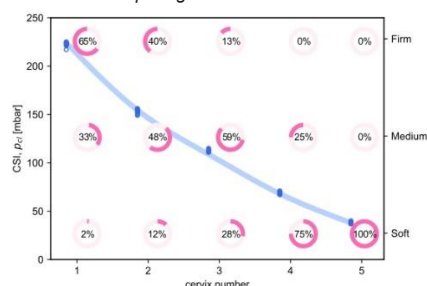
<sup>3</sup>Gynecology and Obstetrics, Thurgau Hospital, Frauenfeld, Switzerland

<sup>4</sup>Department of Obstetrics and Gynecology, University Hospital Basel, Basel, Switzerland

**Problem statement:** Currently, there is no well-established objective technique to assess cervical stiffness during pregnancy. In this work, we compare two methods for cervical stiffness assessment: digital palpation, the standard method used in gynaecology and obstetrics, and a new method based on the aspiration technique. **Methods:** Two methods were used to determine in vitro the stiffness of model uterine cervixes. The stiffness of five model silicone cervixes was assessed using an aspiration-technique based device by five individuals at different time points. Subsequently, 33 obstetricians and 30 midwives assessed the stiffness of each silicone cervix via digital palpation as firm, medium and soft. The silicone cervix models were produced using a 2-component platinum silicone rubber gel. Different stiffnesses, representative of the physiological stiffness at different gestational ages, were achieved by adding a softener to the material at different ratios. **Results:** The inter and intra-observer variability of the two methods was assessed. In the digital palpation test, the participants gave equal judgement only to the softest cervix model, whereas for all the other models their judgements were split among 2 or even all 3 rating possibilities (see Figure). Furthermore, when asked to assess the same cervixes twice, only 24% of the participants did not change their assessment at all, whereas 76% changed the assessment of at least one cervix. In contrast, the maximum relative standard deviation for the device-based stiffness assessment for intra- and inter-observer variability was 3% and 3.4%, respectively. **Conclusion:** The results demonstrate that digital palpation is a subjective and unreliable method to assess cervical stiffness. On the contrary, the device-based on the aspiration technique can help practitioners to assess the cervical stiffness in an objective and reproducible way without the need to rely on their own judgement. Ongoing work will bring evidence to support the use of the aspiration-technique based device as future reliable predictor of premature birth.

**References:** Badir et al. BMC Pregnancy and Childbirth 2020

**Disclosure of Interest:** SB and FD declare competing financial interests as founders of Pregnotia AG. LB declares competing financial interests as employee of Pregnotia AG. The remaining authors declare no competing interests.



Inter-observer variability results of the assessment of all the cervixes (n = 111, 105, 101, 104, 83, respectively). Blue dots represent the assessment made using the device. Pink circles indicate the percentage of participants giving the corresponding assessment (firm/medium/soft).

### AUDIT ON ADHERENCE OF DIAGNOSTIC MODALITIES AND MANAGEMENT PROTOCOL OF PATIENTS PRESENTING WITH SUSPECTED PRETERM LABOUR AT DAY ASSESSMENT UNIT OF A DISTRICT GENERAL HOSPITAL IN UK

Indranil Banerjee

Department of Obstetrics and Gynaecology, Basildon and Thurrock University Hospitals Trust, Basildon, UK

**Problem statement:** It is estimated that around 60,000 babies are born prematurely in the UK every year. This means that 1 in every 13 babies. There has been no decline in the preterm birth rate in the UK over the last 10 years. Babies born preterm have high rates of neonatal and infant mortality, and the risk of mortality increases as gestational age at birth decreases. **Methods:** If the clinical assessment suggests that the woman is in suspected preterm labour and she is 30 weeks pregnant, she can be subjected to treatment for preterm labour without any further diagnostic tests. If Clinical assessment is suggestive and the gestational age is more than 30 weeks :- TVS to determine the cervical length (1st choice) Fetal fibronectin assessment (2nd choice- If TVS not available) The case history of patients presenting in DAY ASSESSMENT UNIT was traced retrospectively and were audited. **Aim:** To look into compliance of our practice compared to our NICE and our local guideline – to find out the loopholes and suggest remedial measures. **Results:** Only 2% of cases presenting in the day assessment unit were offered TVS as the primary modality. Only 2% of cases consultant was informed before admission. 3.100% cases In utero transfer was discussed before admission in cases less than 27 weeks. 4.88% cases FBC and CRP was offered before admission. 5.100% women were offered steroids. 6.75% were offered tocolysis. 7.30% received tocolysis. **Conclusion:** 1. The Trust should identify two or three clinicians to specialize in transvaginal cervical cerclage to enable sufficient capacity for 52 week cover – online FMF training can be beneficial in this case. 2. To increase the GBS coverage, FBC and CRP on admission and tocolysis administration at 100% by 12 months. 3. Preterm labour team consisting of a consultant, registrar and midwife to keep an account of the preterm labour and formulate their prevention strategies and effective management plan as per current guidelines. **Reaudit:** Reaudit to be performed after 1 year to make sure the recommendations have been followed or not.

### HERLYN-WERNER-WUNDERLICH SYNDROME – FEATURES OF DIAGNOSIS AND TREATMENT

Nataliya Veresnyuk<sup>1,2</sup>, Vira Pyrohova<sup>1</sup>

<sup>1</sup>Department of Obstetrics, Gynecology and Perinatology, Postgraduate Faculty, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

<sup>2</sup>Department of Reproductive Health, Lviv Regional Clinical Perinatal Center, Lviv, Ukraine

Herlyn-Werner-Wunderlich syndrome is a complex abnormality in the development of the female genitourinary system, which includes the uterus didelphus, the longitudinal septum of the vagina with obstruction of one half and ipsilateral agenesis of the kidney. The exact prevalence of this syndrome is unknown, but some publications indicate that the frequency of this pathology ranges from 0.16 to 10% among all female genital tract malformations. **Case report:** The article presents a clinical case of a 14-year-old patient with Herlyn-Werner-Wunderlich syndrome, who was diagnosed and treated in time, discusses diagnostic approaches and treatment. The patient complained of progressive dysmenorrhea from the age of menarche within 6 months, which became intolerable and did not pass after receiving symptomatic therapy. Ultrasound examination of the pelvis and kidneys revealed a combined anomaly of the genitourinary system: the uterus didelphus, right hematoocolpos and hemato cervix, agenesis of the right kidney. Magnetic

resonance imaging of the pelvic organs and abdominal cavity confirmed the presence of Herlyn-Werner-Wunderlich syndrome in the patient. Excision of the longitudinal septum of the vagina with the formation of a single vagina was done. During the excision of the septum from the "blind" right vagina, about 200 ml of thick, dark blood was released. There were no intraoperative or postoperative complications. The patient was discharged home in a satisfactory condition on the 5th day. Twelve days after discharge from the hospital, the patient began another menstruation, which lasted 6 days, and was painless. The patient did not express any other complaints.

**Conclusions:** Early diagnosis of Herlyn-Werner-Wunderlich syndrome and its surgical correction will prevent serious gynecological complications. The combined use of expert ultrasound and magnetic resonance imaging plays a decisive role in the diagnosis of this syndrome. The key to success in the management of patients with Herlyn-Werner-Wunderlich syndrome is the coordinated work of a multidisciplinary team with the involvement of a pediatric gynecologist, urologist, radiologist, ultrasound specialist and anesthesiologist. In cases of intrauterine diagnosis of agenesis of one kidney or other pathology of renal development in female fetuses, a differential diagnosis with Herlyn-Werner-Wunderlich syndrome should be made later before the onset of menarche.

## FETOMATERNAL MEDICINE

### VUS IN HRG GENE: A CAUSE FOR RECURRENT MISCARRIAGE, PRETERM LABOUR, IVF FAILURE

Kriti Agarwal, Rajeev Agarwal, Dipanjana Dutta  
Reproductive Medicine, Care IVF, Kolkata, India

**Problem statement:** Although recurrent miscarriage is common, underlying causes can only be determined in about 50% of the cases. Histidine-rich glycoprotein (HRG) is involved in coagulation, angiogenesis and the immunity, all processes that are vital for establishment of a pregnancy. We report a case of recurrent pregnancy loss and preterm labour, in a woman with PCOS, attributed to VUS in the HRG gene.

**Methods:** 33-year-old female partner (P0+5) and 37-year-old male partner, married for 10 years, presented to us with past history of following pregnancy losses: 1. First cycle FET resulted in twin pregnancy, with PPRM at 23 weeks of gestation. 2. Second cycle FET after a year resulted in singleton pregnancy, with spontaneous miscarriage at 16 weeks. 3. Third cycle FET after a year resulted in twin pregnancy with PPRM at 21 weeks, despite cervical encrclage-in-situ. Following, the third miscarriage, hystero-laparoscopy was performed followed by ovarian drilling, adhesiolysis, denomyomectomy, placement of abdominal cerclage. Hysteroscopy revealed a normal cavity. This was followed by 2 IVF-ET failures within a span of another year. She then conceived spontaneously on two occasions, resulting in missed abortion at 6 weeks and 12 weeks respectively. Recurrent pregnancy loss workup including Karyotype, Thrombophilia workup, TORCH, semen DNA fragmentation, hysteroscopy was normal. When she presented to us, we firstly got a genetic consultation done, following which exome testing revealed Variant of Unknown Significance in the HRG gene, which is associated with spectrum of thrombophilia, recurrent miscarriage, hypertensive disorders of pregnancy and placenta accreta spectrum.

**Results:** In view of the above-mentioned complications, couple was given option of surrogacy with either donor eggs or own eggs with PGT-M of embryos. Surrogacy would alleviate the implications of defective placentation and adverse pregnancy outcomes due to this HRG gene. PGT-M of embryos would ensure the embryo free of this mutation would be transferred into the womb of surrogate.

**Conclusion:** Early referral for genetic

consultation and appropriate testing must be considered, early on or at least simultaneously with other workup of recurrent pregnancy loss, by obstetricians, in order to save the couple from unnecessary financial, emotional, physical and age-related fertility losses.

### RUPTURED RUDIMENTARY HORN PREGNANCY MASQUERADING AS CESAREAN SCAR RUPTURE IN THIRD TRIMESTER

Kriti Agarwal, Reetu Hooda  
Obstetrics and Gynaecology, PGIMS, Rohtak, Rohtak, India

**Problem statement:** Pregnancy in the rudimentary horn of a unicornuate uterus is extremely rare and usual fate is rupture in the second trimester. We report a case of rupture of rudimentary horn in the third trimester, which was misdiagnosed as uterine scar rupture.

**Methods:** A 27-year-old G2P1 L1 with previous lower segment Cesarean section presented at 33-week gestation with pain abdomen and syncopal attack with hemodynamic instability. The abdomen was distended and tender, uterine contour could not be made out, fetal parts were felt superficially, and fetal heart sound was absent. On vaginal examination, os was closed, bleeding was absent, and presenting part of the fetus was high up. A provisional diagnosis of uterine scar rupture was made, and the patient was taken up for emergency laparotomy with simultaneous resuscitation.

**Result:** Intraoperatively, a left-sided ruptured rudimentary horn pregnancy and a unicornuate uterus with an intact lower segment transverse scar were found, a 1.5-kg macerated stillborn fetus was lying in the peritoneal cavity, and approximately two litres of hemoperitoneum was present. Excision of the rudimentary horn with ipsilateral salpingectomy was performed.

**Conclusion:** High index of suspicion for uterine malformation is required for cases with a previous history of LSCS for malpresentation. Moreover, catastrophic haemorrhage consequent to ruptured horn pregnancy could have been avoided by excision of the rudimentary horn encountered incidentally in the previous LSCS.

### PREECLAMPSIA: POTENTIAL BIOMARKERS FOR DIAGNOSIS AND TARGETS FOR THERAPY

Ana Alves, Diana Castanheira, Beatriz Ferreira, Barbara Moita, Antonio Santiago  
Gynecology, Leiria Hospital Center, Leiria, Portugal

**Problem statement:** Preeclampsia (PE) is a pregnancy-specific multiorgan disorder, which occurs in 2%–8% of all pregnancies and is a major cause of maternal and perinatal mortality and morbidity. It appears to be due to a defective placental trophoblastic invasion of the uterine spiral arteries, leading to a decrease in uteroplacental blood flow and, consequently, impaired oxygenation that causes the release of substances into the maternal circulation. This process results in an inadequate placental perfusion, oxidative stress, inflammatory response and generalized endothelial damage that affects all organ systems, which translates into several symptoms such as hypertension, proteinuria, increased levels of liver damage markers or even eclampsia with substantial risks to the fetus as placental abruption, iatrogenic preterm delivery, fetal growth restriction (FGR) and perinatal mortality. Therefore, there is an urgent need to identify reliable biomarkers to predict those at risk of developing PE and for effective disease management.

**Methods:** A review literature search of the PubMed database was conducted to identify studies published between 2010 and 2020. The following terms were used and adjusted as necessary: preeclampsia; preeclampsia review; severe preeclampsia; preeclampsia AND pathophysiology; preeclampsia AND diagnostic; preeclampsia AND prevention; preeclampsia AND biomarkers; preeclampsia AND angiogenic factors. Only

articles written in English were considered eligible. Studies were included if they focused on the different biomarkers and their utility in predicting preeclampsia. **Results:** The biomarkers proposed to predict the onset or severity of PE are those that mediate trophoblastic invasion, placental dysfunction, utero-placental circulation and those related to angiogenesis. The most commonly investigated and shown to be promising biomarkers are: pregnancy associated plasma protein A (PAPP-A), placental growth factor (PIGF), soluble fms-like tyrosine kinase (sFlt), placental protein 13 (PP-13), neutrophil gelatinase-associated lipocalin (NGAL), sEndoglin (sEng) and vascular endothelial growth factor (VEGF). **Conclusion:** The combination of potential serum biomarkers with other diagnostic modalities (maternal history, mean arterial pressure (MAP) and uterine artery doppler) could predict the development of PE. An early diagnosis would allow adequate surveillance and clinical management, improving maternal and fetal outcomes. The identification of biomarkers may also generate new target interventions for prevention and treatment of preeclampsia.

#### CONTROLLED BALLON TAMPONADE FOR THE MANAGEMENT OF MASSIVE POSTPARTUM HAEMORRHAGE

**Natalia Artymuk**, Tatiana Marochko, Dmitry Artymuk  
Ob/Gyn, Kemerovo State Medical University, Kemerovo, Russia

**Problem statement:** Massive obstetric haemorrhage remains a significant cause of maternal mortality in all countries. Uterine balloon tamponade has a high success rate for treating severe postpartum haemorrhage and appears to be safe. Objective: to evaluate the effectiveness Zhukovsky's double-balloon obstetric catheter for the controlled balloon tamponade (CBT) in patients with postpartum massive haemorrhage. Materials and Methods. Study design: retrospective, case-control. Group I included 40 patients who used controlled balloon tamponade (CBT) with Zhukovsky's double-balloon obstetric catheter for the management of massive postpartum hemorrhages. Group II (control) consisted of 40 women, to whom this approach was not applied. Primary and secondary outcomes have been determined. The average age of women participating in the study was  $30.65 \pm 6.44$  years and  $32.5 \pm 6.05$  years in Groups I and II, correspondingly ( $p = 0.834$ ). Statistical processing of the results was carried out using the StatSoft Statistica 6.1 application software package license agreement BXXR006D092218FAN11 with determination of the arithmetic mean (M), error of the mean (m) and relative (%) values, Student t-test. Results. Primary and secondary outcomes showed in the table.

Table - Primary and secondary outcomes.

			p
Primary outcomes			
Average volume blood loss, ml	990.6±95.3	1766.6±628.6	0.225
Average volume infusion-transfusion therapy, ml	1863.4±727.5	2278.5±1059.7	0.747
Blood transfusion, abs./%	16 (40.0%)	23 (57.5%)	0.119
Uterine artery ligation, abs./%	17 (42.5%)	6 (15.0%)	0.008
Uterine compression suture, abs./%	13 (32.4%)	3 (7.5%)	0.009
Secondary outcomes			
Duration of hospitalization, days	5.77±2.29	6.75±2.0	0.748
Hysterectomy	2 (5.0%)	13 (32.5%)	0.005

Patients from Group I statistically significantly more often required the use of ligation of the uterine artery 42.5% vs 15.0% and compression sutures in comparison Group II – 15.0% and 7.5% ( $p=0.008$ ,  $p=0.009$ ). However, these patients were significantly less likely to undergo hysterectomy: 5.0% vs 32.5% ( $p=0.005$ ). **Conclusion:** Thus, the use of Zhukovsky's double-balloon obstetric catheter for the controlled balloon tamponade, uterine

compression sutures and ligation of the ascending branch of the uterine artery were an effective method for the treatment of postpartum hemorrhages. Application of this approach allowed a 6-fold reduction in the incidence of postpartum hysterectomy.

#### COVID—19 AND PREGNANCY IN SIBERIA AND FAR EAST

**Natalia Artymuk**<sup>2</sup>, Tatiana Belokrinitskaya<sup>1</sup>

<sup>1</sup>Ob/gyn, Chita State Medical Academy, Chita, Russia

<sup>2</sup>Ob/gyn, Kemerovo State Medical University, Kemerovo, Russia

Despite the increasing number of published studies on COVID-19 in pregnancy, there are insufficient good-quality data to draw unbiased conclusions with regard to the severity of the disease or specific complications of COVID-19 in pregnant women, as well as vertical transmission, perinatal and neonatal complications. The objective of the study was to evaluate an epidemiological characteristic and the course of COVID-19 in pregnant women from the Siberian and Far East Federal Districts of Russia. Materials and methods. The analysis of operational information on the incidence of COVID-19 and the its features in pregnant women and after childbirth provided by the chief obstetrician-gynecologists of the Far Eastern Federal District and Siberian Federal District on May 25, 2020 and August 25, 2020 is carried out. Results. On August 25, 2020, 2010 cases of COVID-19 in pregnant women were detected in two subjects, including 134 active cases. In the population, the proportion of pregnant women among cases of COVID-19 was 1.45%. Pneumonia in pregnant women was registered in 44.8% of cases, severe course of the disease - in 3.7%, hospitalization in RAW - in 1.9% of cases, mechanical ventilation - 0. In the population, pneumonia was registered in 24.4% of cases, hospitalized in RAW - 2.1%, on mechanical ventilation - 0.77%. The incidence in pregnant women was 1451.9 (in the population - 599.8). 23 (1.76%) COVID-19 (+) newborns were identified, despite preventive measures and separation of mother and child immediately after childbirth, which does not exclude vertical transmission of the disease. Maternal mortality was 2 cases (0.1%) vs population mortality 1.75. Perinatal mortality was 7 cases (0.35%). There were 5 (0.25%) stillbirths. Early neonatal mortality was 2 (0.1%) cases. Conclusion. The incidence of COVID-19 in pregnant women in Siberia and the Far East is higher than in the general population with a higher incidence of pneumonia, but a milder course: less need for ICU, mechanical ventilation and mortality. 23 cases of COVID positive newborns, despite the separation of mother and child, do not exclude the possibility of vertical transmission of infection.

#### AN AUDIT OF CAESAREAN SECTION FOR ARREST OF ACTIVE PHASE LABOUR AND THE USE OF OXYTOCIN AT TWEED HOSPITAL

**Jessica Benton**, Steve Abbey

Medicine, Bond University, Gold Coast, Australia

**Problem Statement:** Oxytocin is widely used to augment arrested active labour when labour does not progress at an adequate rate. A caesarean section is often performed for abnormal labour progression, due to the belief that full dilation and vaginal delivery would otherwise be prolonged and incur adverse health outcomes. This audit aimed at assessing the prevalence and associated complications of caesarean for arrested labour and the use of oxytocin in women delivering at term at the Tweed Hospital. **Method:** An audit was conducted between January 2017 and June 2020, retrospectively examining the eMaternity database. Groups were compared in a non-adjusted analysis using non-parametric Kruskal-Wallis and Pearson's chi-squared, with a significance level of 0.05. A total of 3,908 deliveries were examined, with 358 nulliparous women included.

**Results:** The rates of nurse admission or APGAR score at 5 minutes did not differ in babies delivered by emergency caesarean for arrest of labour, compared with an elective caesarean. Maternal blood loss during delivery was significantly higher in caesarean deliveries for arrest of labour compared with foetal distress and elective caesareans. The prevalence of caesarean for arrest of labour was found to be 49%, of which 100% received oxytocin. **Conclusion:** This audit highlights that oxytocin is a presumed requirement for the diagnosis of arrested labour, with all women with arrested labour given oxytocin before a decision for caesarean. Further study is necessary to examine all caesarean sections for foetal distress, to determine whether arrest of labour was also present and if diagnosed earlier, may have avoided undue newborn distress.

#### PLACENTAL ANATOMOPATHOLOGICAL STUDY IN CASES OF THREAT PRE-TERM DELIVERY

Sara Bernardes Da Cunha<sup>1</sup>, Patricia Ferreira<sup>1</sup>, Carolina Carneiro<sup>1</sup>, Ines Reis<sup>1</sup>, Catia Rasteiro<sup>1,2</sup>, Augusta Pinto<sup>1</sup>, Teresa Teles<sup>1</sup>

<sup>1</sup>Gynecology and Obstetrics, Centro Hospitalar De Entre Douro E Vouga, Feira, Portugal

<sup>2</sup>Faculdade De Ciencias Da saude, Universidade Da Beira Interior, Covilha, Portugal

**Problem statement:** Preterm delivery (PTD) has a known multifactorial etiology. In cases of preterm delivery threat (PTDT) it isn't well known why some of the labors occurs and others don't. The anatomopathological placental exam (APE) gives the opportunity to take a look into the intra-uterine environment. The purpose of our work is compare and analyze APE and newborn weight at birth in the cases of PTDT with and without effective PTD. **Methods:** A descriptive and retrospective study was conducted evolving the cases of PTDT of our unit. Evaluation of maternal sociodemographic data and information from delivery, newborn and APE. The cases were divided in two groups, between effective PTD (previous to 37 weeks of gestation) – group 1- or cases with PTDT with delivery after 37 weeks of gestation – group 2. The two groups were compared. **Results:** 97 cases were selected to analysis. The mean gestation age was 34 weeks. In the selected samples 38 APE were conducted. In group 1 the most common placental histology find was chronic villitis, insufficient maternal perfusion and chronic chorioamnionitis in 45% of cases. In the group 2 these findings were present in 42% of cases. Chorioamnionitis was found in 25% of PTD and 14% of the second group. In the cases where placental anatomopathology was accessed, there is a statistical significant difference on birth weight percentile between groups ( $t=7,312$ ;  $p=0,012$ ). The proportion of cases with fetal growth restriction was higher in group 1 ( $X^2(1)=6,83$ ;  $p=0,03$ ). **Conclusion:** Although the sample size limitations, there was a higher proportion of chorioamnionitis in the cases of PTD in relation to PTDT with delivery after 37 weeks. The fetus with younger gestation age at delivery had lower weight percentile and more cases of fetal growth restriction so the placental histological alterations could be related with the PTD. One important limitation of our study was the few cases of APE of PTDT with term delivery, which leads to a less effective comparison.

#### UPTAKE AND OUTCOMES OF VAGINAL BIRTH AFTER CAESAREAN (VBAC) IN NHS LANARKSHIRE

Edie Booth, Samuel Enokela, Annapurna Pandravada, Amr Gebril, Ekram Abdelseid  
Obstetrics, University Hospital Wishaw, Glasgow, UK

**Problem statement:** There is evidence that robust discussion and motivation encourages uptake of VBAC. Given the increasing caesarean section rate globally we

aimed to review antenatal practice in NHS Lanarkshire to identify areas for improvement of VBAC uptake and to fully inform women in antenatal counselling. **Methods:** We reviewed the electronic records of 340 women delivering between June and December 2019 who had at least one previous caesarean section. Exclusion criteria: 1 previous caesarean, second trimester miscarriage, breech or medical conditions which absolutely contraindicated planned VBAC. Records were manually reviewed and findings entered into a pre-designed Microsoft excel proforma and analysed. **Results:** VBAC uptake rate was only 28% however success rate was 76%. VBAC success was greater in those with a previous vaginal delivery (89%). There were similar success rates between spontaneous labourers (21%) and those induced (25%). Indications for emergency caesarean included failure to progress, fetal distress, scar pain and failed forceps. No women had a uterine rupture. Maternal complications included post-partum haemorrhage, second degree tear, sepsis and wound infection. Similar complication rates between elective caesarean (31%) and VBAC (29%) were noted. Emergency caesarean had the highest complication rate (50%). Those induced had higher maternal complication rates than spontaneous labourers (29% vs 11%). 50% of women had no clear documentation of antenatal leaflet given and only 57% of women eligible for VBAC had clear MOD discussion documented. **Conclusion:** The results highlighted low uptake of VBAC alongside poor documentation of antenatal discussion on MOD but with success rates comparable to national standards. We concluded that dedicated multidisciplinary consultant led VBAC clinics may improve VBAC uptake by offering MOD discussion including a local statistics leaflet, VBAC booking checklist and focussed antenatal counselling. This should ensure that eligible women are identified early to aid well informed decisions. We aim to re-audit following implementation of the above changes. In light of the increasing global caesarean section rate we wonder whether women with one previous section and no contraindications to vaginal delivery should be offered VBAC as first line MOD?

#### ACTIVE TERMINATION OF TERM PREGNANCIES IN FETAL GROWTH RESTRICTION - QUESTIONING CURRENT PRACTICES

Joao Coimbra, Ana Rita Mateus, Vera Mourinha, Ana Paula Silva

Departamento De Obstetricia E Ginecologia, Centro Hospitalar Universitario Do Algarve - Unidade De Faro, Faro, Portugal

**Problem statement:** Fetal growth restriction (FGR) can be diagnosed by ultrasound in all fetuses with an estimated fetal weight below the 3rd percentile adjusted for gestational age. Following the former diagnose, current international guidelines on fetal medicine advise on active termination of pregnancy (most commonly by labor induction) at different specific gestational timings, but for all cases before the 41st week of pregnancy. Considering the underdiagnosis of fetal growth restriction, active termination of pregnancy according to these guidelines is often neglected, allowing for comparison between clinical practices. **Methods:** All deliveries of Hospital de Faro between the years of 2016-2019 with at least 37 weeks of gestational age and FGR (as defined by birth weight below de 3rd percentile were included in the study, accounting for 212 cases. Birth weight percentiles were obtained using the INTERGROWTH-21 formulae. Comparison was made between the fetuses who undergone active termination of pregnancy between the 37th and 40th week (and 6 days) specifically due to the FGR diagnosis and those fetuses which did not. Clinical outcomes selected for comparison were: gestational age at birth, incidence of birth by caesarian section, Apgar score 7 on the 1st and 5th minutes and incidence of neonatal intensive care unit admission at

birth. Statistical significance was considered for p value 0,05. **Results:** For those fetuses with active termination of pregnancy specifically due to the diagnosis of FRG, gestational age at birth was lower ([38,1-38,8] IC 95% vs [39,4-39,8] IC 95%); and incidence of neonatal intensive care unit admission at birth was higher (p=0,04). No statistical differences were found for incidence of birth by caesarian section (p=0,25), Apgar score 7 on the 1st minute (p=0,14) or Apgar score on the 5th minute (p=0,31). **Conclusion:** Active termination of pregnancy at term specifically due to FGR may have a negative impact on neonatal clinical outcomes. A future study using more cases is pertinent.

## PREGNANCY LOSS, RANDOM EVENTS AND COSMIC RAYS

Piet C de Groen

Academic Health Center, University of Minnesota, Minneapolis, USA

**Problem statement:** Recent genome-wide association studies have identified over 220 genetic variants that are associated with menopause; the majority of variants are involved in DNA repair and maintenance. We discovered that distribution of one or more neoplasia among cases follows a predictable pattern of random events that are modeled by omnipresent neoplasia equations (ONE). A natural but controversial explanation of random DNA events is that cosmic rays, in particular secondary cosmic rays, induce DNA mutations. **Aim:** To determine whether the ONE model pregnancy loss (PL) assuming random DNA mutations. **Methods:** We searched the literature for case series describing one or more PLs per case. The following ONE were used: (1)  $f(p) = X^p / (\sum_{p=0}^{\infty} X^p)$  – the fraction in the population at risk for PL with chance X for a specific value of p; and (2)  $f(x) = A / (1 + e^{(-k \cdot (x - x_0))})$  – the expected incidence in year x for PL with a maximum incidence A, a slope x0 and a midpoint of k year. The congruency of observed and modeled data was analyzed by Pearson correlation coefficient (PCC); a PCC 0.9995 was rounded up to 1.0. **Results:** Five PL studies were identified containing numeric data. ONE (1) modeled observed data with perfect accuracy; the combined PCC for the five studies was 1.0 (Figure 1A). Next, we modeled PL incidence; we considered three components. The first component was oocyte failure by cosmic rays starting at birth and completed by age 90 using ONE (2). The second component was any form of non-oocyte injury or disease using the same logistic equation starting at birth and completed by age 120. The third component was environment, a constant factor. The model predicted the following average PL frequencies (age/%): 20/13, 25/14, 30/16, 35/22, 40/38; ovarian failure or menopause occurred around age 51. A comparison with the 2000 PL study of Denmark showed a PCC of 0.999 (Figure 1B). **Conclusion:** The ONE allow modeling of observed population PL with astounding accuracy and predict a PL frequency of 16% at age 30 and menopause around age 51. The main cause of PL may be continuous DNA injury by cosmic rays causing cumulative oocyte failure.

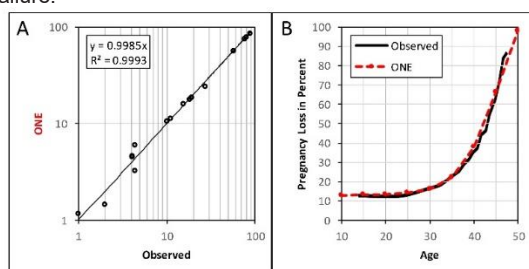


Figure 1. A: Observed vs. modeled (ONE) data comparing measured versus estimated PL distribution. B: Observed vs. modeled (ONE) PL incidence by age.

## DO VEGETARIAN PREGNANT WOMEN NEED FOOD SUPPLEMENTS?

Natalia Del Valle Sanchez Baudo, Silvia Morales Munoz, Esmeralda Lopez Lopez

Obstetricia y Ginecología, Hospital De Poniente, El Ejido, Spain

**Introduction:** Adequate nutrition is essential for optimal fetal development. Currently, there is a growing number of vegetarians in society. **Problem:** To carry out a review about influence of vegetarian diet on perinatal and maternal outcomes; to be able to provide advice and offer nutritional supplementation when it is necessary. **Methodology:** A review was carried out in Pubmed and Uptodate with the keywords "vegetarian diet" AND "pregnancy" AND "outcomes", published in English during the last 10 years. Thirteen articles were found, choosing 4 of interest. **Results:** All the studies consulted confirm that vegetarian diet is safe during pregnancy, although more studies are necessary to probe a relationship between phytoestrogens and hypospadias in men. There is short evidence about no differences between varied vegetarian diet and omnivorous one in terms of birth weight and weeks of gestation. **Conclusions:** Vegetarian diet appears to be safe during pregnancy. Vegetarian pregnant women should be candidates to need iron, vitamin B 12, and omega3 supplementation depending on their diet restrictions.

## A SUCCESSFUL PREVENTION OF PRE-ECLAMPSIA WITH ASPIRIN, VITAMIN D AND CALCIUM SUPPLEMENTATION – A CASE REPORT

Emina Ejubovic<sup>1,2</sup>, Malik Ejubovic<sup>3</sup>, Ivka Djakovic<sup>4</sup>, Nika Oreskovic<sup>5</sup>

<sup>1</sup>Department of Gynecology and Obstetrics, Cantonal Hospital Zenica, Zenica, Bosnia and Herzegovina

<sup>2</sup>Department of Gynecology, Obstetrics and Reproductive Medicine, Sarajevo Medical School, Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina

<sup>3</sup>Department of Internal Diseases, Cantonal Hospital Zenica, Zenica, Bosnia and Herzegovina

<sup>4</sup>Department of Gynaecology and Obstetrics, Sestre milosrdnice University Hospital Center Zagreb, Zagreb, Croatia

<sup>5</sup>Department of Emergency Medicine in Zagreb County, Department of Emergency Medicine in Zagreb County, Velika Gorica, Croatia

**Problem statement:** It has been shown that, in pregnancies which are at high-risk for pre-eclampsia (PE), an administration of aspirin in the dosage of 150 mg/day reduces the early-onset of PE, as well as the preterm delivery at 37 weeks and intrauterine growth restriction (IUGR). Additionally, there was a small and insignificant effect of aspirin on the incidence of term PE. Furthermore, in women with low calcium intake, a supplementation with calcium may prevent both the early and the late-onset of PE while women taking supplements containing vitamin D had a lower risk of developing pre-eclampsia. **Methods:** This is a case report. The aim of this case report is to present a successful prevention of pre-eclampsia with aspirin, vitamin D and calcium. **Results:** A G3P2 woman was referred to a gynecologist after a positive pregnancy test for a regular check-up. Her first pregnancy was uneventful, while her second pregnancy was complicated with the risk of premature labor, pregnancy induced hypertension (PIH) and PE. During her first check-up, a blood pressure (BP) of 140/95 mmHg was recorded. An ultrasound examination has shown a fetus measuring 34,8mm crownrump length (CRL)—10+2 weeks gestation, while a Doppler sonography has revealed uterine notching which was suggestive for PIH and PE. An aspirin in the dosage of 100 mg/day, 2400 international units (IU) of vitamin D and calcium supplementation were prescribed for the patient. The patient was thoroughly monitored during the whole pregnancy, with regular laboratory and BP monitoring which were always normal. The BP prior the delivery was 140/95 mmHg and she delivered a healthy baby girl at term, which weighted 3960 grams and was 52cm long, Apgar score was

8/9. **Conclusion:** This case report presents a successful prevention of PE with aspirin, vitamin D and calcium supplementation in a patient with positive history of PIH and PE and a uterine notching on Doppler sonography. Furthermore, with this therapy, a premature labor, the IUGR and the adverse neonatal outcome were also prevented. This therapeutic scheme might be used successfully from the first trimester in cases where there are risk factors for developing PE.

#### APLASIA CUTIS CONGENITA ON LUMBOSACRAL AREA - A CHALLENGING DIFFERENTIAL DIAGNOSIS

Patricia Ferreira<sup>1</sup>, Ines Reis<sup>1</sup>, Susana Saraiva<sup>1</sup>, Vania Ferreira<sup>1</sup>, Margarida Gameiro<sup>1</sup>, Miguel Branco<sup>2</sup>, Carla Pina<sup>1</sup>

<sup>1</sup>Obstetrics and Gynaecology, Centro Hospitalar de Entre Douro e Vouga, Ovar, Portugal

<sup>2</sup>Obstetrics and Gynaecology, Maternidade Bissaya Barreto, Coimbra, Portugal

**Introduction:** Aplasia cutis congenita (ACC) is a rare condition with an estimated incidence of about 1 to 3 10.000 live births. It is a heterogeneous group of disorders characterized by well-circumscribed focal absence of epidermis, dermis, and occasionally subcutis at birth. The exact mechanism for developing ACC is still not completely understood. Genetic factors, teratogens, compromised vasculature to the skin and trauma are believed to play a role in this matter. Some authors consider ACC a mild form of a neural tube closure defect. This report shows the challenge in the prenatal diagnosis, particularly in the exclusion of neural tube defects. **Report:** A 38-year-old and primigest woman. Non-consanguineous couple. Routine prenatal sonography performed at 20 weeks gestation identified a hypoechoic cystic structure with 11 mm x 2,3 mm at the level of the lumbar region, without meningeal or cranial neural tissue. Fetal neurosonography and MRI confirmed a cutaneous cystic image at L3 level, avascular, with no continuity with the spinal canal. Genetics studies (QF-PCR and Array-cGH analysis) were unremarkable. In the 3rd trimester ultrasound, the lesion decreased slightly. Fetal echocardiography at 32 weeks did not reveal any changes. Neonatal physical examination revealed an atrophic lesion in lumbar region similar to a membranous scar. It had a well demarcated margin and diameter of 3 cm. It was associated with several telangiectasias in the center and peripherally. The neonate had normal neurologic examination findings, and no additional major or minor congenital abnormalities were noted. **Conclusion:** Fetal neurosonography and MRI are crucial to exclude the involvement of the central nervous system. The diagnosis of ACC is based on the clinical findings after birth. This case suggests membranous ACC that is distinguishable from nonmembranous ACC by its well delimited borders and scaly surfaces. Membranous ACC does not have a familial inheritance pattern and is unlikely to be associated with other nonneuroectodermal anomalies. This fact is essential for postnatal counseling.

#### ADVANCED MATERNAL AGE AND LOW BIRTH WEIGHT

Patricia Ferreira, Susana Saraiva, Ines Reis, Matilde Martins, Vania Ferreira, Augusta Pinto, Teresa Paula Teles  
Obstetrics and Gynaecology, Centro Hospitalar De Entre Douro E Vouga, Santa Maria Da Feira, Portugal

**Introduction:** Increasing maternal age has been a worldwide trend. Socio-economic and labour changes have conditioned a significant increase in the number of women who postpone maternity. In Portugal, between 2000 and 2019, the average age of the mother at birth of her first child increased about 4 years, reaching 30.5 years. Advanced maternal age may be associated with worse neonatal outcomes, namely low birth weight (< 2500 grams). **Methods:** A retrospective cohort study was conducted between 2016 and 2019 in a level II hospital. The inclusion

criteria were defined: maternal age  $\geq 20$  years; birth after 24 weeks and weight over 500g. And the exclusion criteria: multiple pregnancy, fetal malformation and intrauterine fetal death. The chi-square test was used to compare categorical variables and the multinomial logistic regression to adjust for confounding variables. **Results:** Of the 6351 births in the mentioned period, a final number of 5716 were obtained, and distributed according to the following: 782 from 20-24 years; 1515 from 25-29 years; 1894 from 30-34 years; 1231 from 35-39 years; 294 from  $\geq 40$  years. Chronic hypertension, gestational hypertension and gestational diabetes are statistically significant associated with increased maternal age. The low birth weight rate was highest in the 35-39 age group (23.6%) and lowest in the 20-24 age group (0.4%). After adjustment for confounding variables, the low birth weight odds ratio for the 35-39 age group was 1.091 (95% CI; 0.775-1.538) and for the  $\geq 40$  years was 0.530 (95% CI; 0.344-0.816). **Conclusion:** Although the low birth weight rate was higher in the 35-39 age group, when adjusted for the confounding variables, it is in the age group  $\geq 40$  years that there is the highest risk for this outcome.

#### CERVICAL ADENOCARCINOMA IN SITU DIAGNOSED IN A LATE SECOND TRIMESTER PREGNANCY: A CASE REPORT

Mariana Lira Morais, Mario Moura, Cristina Alves, Ana Moreira, Zelia Gomes, Osvaldo Moutinho

Gynecology/Obstetrics, Centro Hospitalar Tras os Montes e Alto Douro, Vila Real, Portugal

**Problem statement:** Adenocarcinoma *in situ* (AIS) of the uterine cervix is a precursor of cervical invasive disease and its incidence has increased over the past few decades. The incidence of gynecological malignant tumors during pregnancy has increased, mainly due to the greater number of older age pregnancies. Treatment of preinvasive disease during pregnancy is questionable but might be deferred to the postpartum period. **Case Report:** We report a 28-year-old pregnant woman, primigravida, non-smoker and first intercourse at 17 years. She had no previous gynecological surveillance. From her clinical record, HCV chronic infection is the only relevant issue. She underwent pap smear at the 16th week of pregnancy and the result was high-grade intraepithelial lesion (HSIL). She was referred to our cervical pathology unit and her first assessment was at 24 weeks of gestation. Gynecological examination showed no macroscopic changes in vulva, vagina and cervix. An adequate colposcopy was performed and demonstrated a type 1 transformation zone and grade 2 colposcopic findings, without suspected invasion. Cervical biopsy was guided by colposcopy and revealed conventional *in-situ* endocervical adenocarcinoma. Another colposcopy was performed at 35 weeks, without the need of a new biopsy. Delivery occurred at 38 weeks by cesarean section after a failed attempt to induce labor. A healthy girl was born with 2950 grams and an Apgar score 9/10. Cervical loop electrosurgical excision was performed to make the definite diagnosis and was scheduled for 8 weeks postpartum. Histology revealed lesions of AIS in the endocervical side and HSIL/CIN3 in the exocervical side. Borders were free of dysplastic epithelium. **Conclusion:** Coexistence of cervical adenocarcinoma and HSIL is relatively frequent given the shared etiology (HPV). In this case, HSIL was the finding that lead to the detection of cervical AIS. Both fetal and maternal factors should be considered when deciding the option of treatment. At this gestational age, cervical conization should not be performed mainly due to the risk of hemorrhage, premature rupture of membranes, preterm labor and infection. Management of the cervical AIS biopsy result during pregnancy remains controversial, especially because a biopsy cannot rule out the presence of invasive disease.

## PERIVIALE BIRTH: CAUSES AND RECURRENCE RISK

Ana Rita Mateus, Diana Almeida, Ana Paula Silva, Joao Coimbra  
Obstetrics service, Centro Hospitalar Universitario do Algarve, Faro, Portugal

**Problem statement:** Approximately 0.5% of all births occur before the third trimester of pregnancy, and these very early deliveries result in the majority of neonatal deaths and in more than 40% of infant deaths. The main objective was to characterize the main causes of periviable birth and to determine whether periviable birth can be predicted by previous pregnancy outcome. **Methods:** Retrospective study that included 12548 pregnancies, which took place between January 2015 and March 2020, at the Centro Hospitalar Universitario do Algarve – Faro Unit. All periviable births were evaluated (between 20 weeks and 0 days of gestation and as 26 weeks and 6 days of gestation) determining their frequency and the main causes of admission in this subgroup of pregnant women. **Results:** Periviable birth was found in 0.35% of all births that occurred in this period of time, with 4.5% of those occurring below 23 weeks of gestation. Thirty-four percent of these women had a history of previous abortion or fetal death and 33% of the multiparous women included in the study had a history of previous preterm birth. The main causes of periviable birth were premature rupture of membranes (38.6%), vaginal bleeding (13.6%) and pre-eclampsia (4.5%). About 18% of pregnancies were multiple. There was also the presence of maternal pathology in 21% of these pregnant women, the most frequent being hypothyroidism, diabetes and urinary tract infections. An anatomopathological study of 75% of these placentas was performed and it was found that chorioamnionitis was present in 52.3% and placental insufficiency in 11.4%. **Conclusion:** There was a statistically significant association between the existence of maternal pathology and a lower birth weight of the newborn. The existence of previous preterm delivery has been associated with periviable deliveries for earlier gestational ages. Despite this last association, and according to the literature, preterm or periviable birth or periviability in a previous pregnancy are insensitive markers of recurrence in a subsequent pregnancy.

## PERIVIALE BIRTH - MODE OF DELIVERY

Ana Rita Mateus, Diana Almeida, Ana Paula Silva  
Obstetrics Service, Centro Hospitalar Universitario Do Algarve, Faro, Portugal

**Problem statement:** The optimal way of delivery in situations of periviability has been the subject of considerable discussion and controversy. On the one hand, cesarean section can improve the neonatal outcome by ensuring greater readiness for access to neonatal intensive care, on the other, this route has also been associated with worse maternal outcomes. The main objective was to determine the frequency of vaginal and cesarean delivery and evaluate postnatal results in situations of periviability. **Methods:** Retrospective study that included 12548 pregnancies, which took place between January 2015 and March 2020, at the Centro Hospitalar Universitario do Algarve – Faro Unit. All periviable births were evaluated (between 20 weeks and 0 days of gestation and as 26 weeks and 6 days of gestation) and all newborns were characterized in terms of weight, Apgar score, hospitalization and survival. **Results:** Periviable birth was found in 0.35% of all births that occurred in the considered period of time, with 4.5% of those occurring below 23 weeks of gestation. Vaginal deliveries were performed in 63.6% of pregnant women, with the remaining undergoing cesarean section. Fetal presentation showed an extremely significant

association with the choice of delivery type (vaginal delivery: 89.3% cephalic presentation vs 10.7% breech presentation, cesarean section: 37.5% cephalic presentation vs 62.5% breech presentation;  $P < 0.001$ ). The average birth weight was 758 g (400-1260 g) and the average 5-minute Apgar scores was 6. There were 22.7% stillbirths (9.1% males and 13.6% females). An average length of hospital stay of 63 days was observed, with 20.5% of newborns being transferred to other units. **Conclusion:** No association was found between the mode of delivery and the length of hospital stay or the occurrence of death at birth. A current survival of only 54.5% was found in these children.

## FETAL GROWTH RESTRICTION (FGR): MORE THAN LOW BIRTHWEIGHT; MEASURES OF ASYMMETRIC FGR BETTER DEFINE THE GROUP 'AT RISK' GROUP THAN LOW BIRTHWEIGHT FOR GESTATIONAL AGE (SGA)

Roger McMaster-Fay, Jon Hyett, Bradley De Vries  
RPA Womens and Babies, University of Sydney Medical School, Camperdown, Australia

It is thirty years since we demonstrated that infants with asymmetric FGR had poorer outcomes than those with SGA at term with higher caesarean section and fetal distress (including stillbirth) rates.<sup>1,2</sup> We used Ponderal index (PI), a measure of birthweight (BWt) for length, to quantitate asymmetric FGR. [Figure 1.] Despite these findings most still use BWt centiles as their measure of FGR. Asymmetric FGR is also known as 'brain sparing' FGR or Placental-Fetal GR3 as it is mainly secondary to placental vascular disease and results in shunting of blood to the brain in the fetal circulation. Thus, cerebroplacental Doppler ratio studies have been found to be useful in defining this group. Another useful measure of asymmetric FGR may be the ratio of BWt to head circumference (HC): The Brazilians (Goncalves et al.),<sup>4</sup> used a BWt/HC ratio of  $\geq 0.9$  to define disproportionate (asymmetric) fetal growth in a study of 915 term infants. On measuring their chest circumference, arm circumference and triceps skinfold thickness, they found these infants had other indicators of fetal wasting. The Dutch found that comparing BWt and HC was useful in defining asymmetric FGR groups of preterm and very preterm infants, which PI does not.<sup>5</sup> Bocca-Tjeerets et al.<sup>5</sup>, in a study of 810 preterm infants, defined asymmetric FGR as any newborn infant with a BWt z-score more than 1SD different to its corresponding HC z-score. Using this formula defined 11% of infants born between 35 and 32 weeks and 10% between born between 31 and 25 weeks gestation. With this formula it is possible to have outcome measures of asymmetric FGR for both term and preterm infants. We plan to analyse these different measures on a large data-base but this has been delayed because of the COVID-19 pandemic.

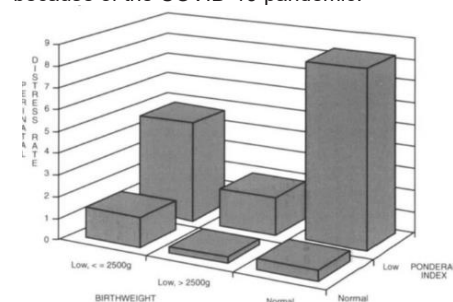


Figure 1. Rates of perinatal distress in relation to Ponderal index and birthweight, from data in Villar et al.<sup>1</sup>

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### THE REBOA TECHNIQUE TO REDUCE MORBIDITY IN PATIENTS WITH KNOWN PLACENTA ACCRETA SPECTRUM DISORDERS: A CASE SERIES

Sharron Moeraert, Anne Loccufier, Eva-Line Decoster, Filip Vandenbrande, Philippe Van Trappen  
*Gynaecology-Obstetrics, AZ Sint-Jan, Bruges, Belgium*

**Problem statement:** Placenta Accreta Spectrum (PAS) disorders refer to the penetration of trophoblastic tissue through the decidua basalis into the underlying uterine myometrium, the uterine serosa or even beyond, extending to pelvic organs. The incidence of this pathology has increased due to the rise in cesarean section rates. There is no consensus concerning the management of these pregnancies. Cesarean hysterectomy for the treatment of PAS disorders has the potential to be associated with significant blood loss, massive transfusion, and operative morbidity. Here we report a technique to reduce these risk factors in co-operation with the endovascular surgical team: the 'Resuscitative Endovascular Balloon Occlusion of the Aorta' (REBOA) technique. **Methods:** This case series describes two patients diagnosed with Placenta percreta in pregnancy scheduled for an elective cesarean, followed by hysterectomy. This surgical technique utilizes the placement of the REBOA with the balloon placed above both arteria renalis, under general anesthesia just before incision. The balloon is inflated immediately after clamping of the umbilical cord, then mobilised under the arteria renalis 4 to 5 minutes later, after clipping/ligating the uterine arteries laterally and the vessels in the ovarian ligament and finally deflated when hysterectomy was completed. The following surgical outcomes were collected: operating time (minutes), estimated blood loss (EBL), intraoperative complications, need for reoperation before discharge, and transfusion rates. **Results:** In these 2 cases, an operating time was seen of respectively 22 and 35 minutes for cesarean + hysterectomy, and in both 60 minutes from opening of the abdomen until closing. The estimated blood loss was respectively 2000cc and 300cc, there were no intra-operative complications, no need for re-operation before discharge and no blood transfusion was needed. **Conclusion:** The REBOA technique, used as described above, during cesarean hysterectomy can significantly reduce blood loss and transfusion rates, as well as operating time. This technique is applicable especially in the non-emergent setting. No side effects were seen in short or long term as a result of the REBOA technique, except the (unavoidable) hysterectomy. Further research is needed to standardize the management of PAS.

### DELIVERY ROUTE IN PREGNANT WOMEN WITH PREVIOUS CESAREAN SECTION IN OUR HOSPITAL

Silvia Morales Munoz, Esmeralda Lopez Lopez, Natalia Sanchez Baudo  
*Obstetricia Y Ginecologia, Hospital De Poniente, El Ejido, Spain*

**Problem:** To analyze in a descriptive way the method of termination of labor (caesarean section, eutocic or instrumental vaginal delivery) in pregnant women with previous caesarean section in our Service in 2019. **Methods:** Retrospective searching in our hospital database (Ariadna) of those pregnant women with a previous cesarean section, classifying them according to their delivery route in current pregnancy (vaginal delivery or second cesarean section in this pregnancy). It has also been analyzed how many required instrumentation, and

what instrument was applied. **Results:** During the year 2019 2,678 births occurred in our Service: 2,179 vaginal deliveries (81.4%), and 499 cesarean sections (18.6%). Of the vaginal deliveries, 56.6% had a previous cesarean section. Of these, 45.2% were eutocic, while instrumentation was necessary in 11.4% (6.6% suction cup, followed by 2.1% spatulas and 0.7% forceps). **Conclusions:** Vaginal delivery after a previous cesarean section is frequent in our Department. Almost half of these deliveries with a history of previous cesarean section did not require any type of instrumentation. The instrument most applied in these pregnant women was the obstetric vacuum cup. Performing a routine elective cesarean section after a previous cesarean section increases maternal morbidity and mortality and generates a high healthcare cost.

### PRENATAL DIAGNOSIS OF SPLIT SPINAL CORD MALFORMATION TYPE 1 – TWO DIFFERENT CASES, ONE SAME OUTCOME

Sara Nunes<sup>1</sup>, Marta Campos<sup>2</sup>, Catia Lourenco<sup>2</sup>, Monica Melo<sup>2</sup>, Joana Nunes<sup>3</sup>, Cristina Godinho<sup>2</sup>, Conceicao Brito<sup>2</sup>  
<sup>1</sup>Gynecology & Obstetrics, Centro Hospitalar Tras-os-Montes e Alto Douro, Vila Real, Portugal  
<sup>2</sup>Gynecology & Obstetrics, Centro Hospitalar Vila Nova de Gaia/ Espinho, Vila Nova de Gaia, Portugal  
<sup>3</sup>Medical Imaging, Neuroradiology Unit, Centro Hospitalar Vila Nova de Gaia/ Espinho, Vila Nova De Gaia, Portugal

**Problem statement:** Split spinal cord malformation type 1 (SSCM1) or diastematomyelia occurs when there is a longitudinal division that splits the spinal cord into two hemi-cords. It's considered a spinal dysraphism and may be associated with other anatomic anomalies. Major concern is neurologic dysfunction and progressive neurologic impairment of lower extremities and rectal/vesical sphincters which is difficult to predict before birth. Authors present two cases of prenatal diagnosis of SSCM1 with different imaging findings. **Methods:** Information was obtained from medical records. **Results:** The first case, in 2013, is from a 32-year-old nulliparous woman with a dichorionic twin pregnancy after in vitro fertilization. Second trimester ultrasound revealed right clubfoot and thoracolumbar scoliosis with lumbar hemivertebrae in the second twin. Karyotypes were normal in both fetuses. Fetal magnetic resonance imaging (MRI) confirmed single twin anomalies but could not differentiate diastematomyelia from segmental spinal dysgenesis. Selective feticide was performed at 30 weeks and cesarean occurred two weeks later because of spontaneous preterm labour and chorioamnionitis. Fetal autopsy confirmed diastematomyelia with spina bifida occulta. The living twin has had a normal neurocognitive development so far. The second case, in year 2020, occurred in a 30-year-old nulliparous woman with a spontaneous unifetal pregnancy. First trimester ultrasound and biochemical screening were normal but at 21 weeks, an isolated spinal echogenic focus was detected in fetal lumbar region. MRI confirmed occult spinal dysraphism with a lumbar osseous spur and a tethered cord couldn't be excluded. Fetal array comparative genomic hybridization (aCGH) study was normal. After clinical discussion with pediatric neurologist, parents chose to terminate pregnancy, at 23 weeks. Final fetal autopsy is not yet available. **Conclusion:** Being SSCM an uncommon congenital malformation with unpredictable neurologic impairment, prenatal counseling remains challenging. Multidisciplinary teams are important to discuss and counsel parents of fetuses affected with this rare type of spinal malformation. *No conflict of interest to declare.*

## PERIPARTUM CARDIOMYOPATHY, A RARE CAUSE OF POSTPARTUM DYSPNEA

Sara Nunes<sup>1</sup>, Fernando Goncalves<sup>2</sup>, Mariana Morais<sup>1</sup>, Cristina Alves<sup>1</sup>, Mario Moura<sup>1</sup>, Rosario Almeida Lopes<sup>1</sup>, Osvaldo Moutinho<sup>1</sup>

<sup>1</sup>Gynecology & Obstetrics, Centro Hospitalar Tras-os-Montes e Alto Douro, Vila Real, Portugal

<sup>2</sup>Cardiology, Centro Hospitalar Tras-os-Montes e Alto Douro, Vila Real, Portugal

**Problem statement:** Peripartum cardiomyopathy (PPCM) is a type of dilated cardiomyopathy that develops in late pregnancy or during the first 5 months postpartum. Incidence rates vary widely (1:100 – 20 000 pregnancies) and diagnosis is based on exclusion of other causes of cardiomyopathy. More than 30% don't completely recover left ventricular function which contraindicates a future pregnancy. The authors present one such case of PPCM with incomplete recovery. **Methods:** Information was obtained from medical records. **Results:** From 6590 deliveries between 2015 and 2019, there was one case of PPCM registered in our center in 2017. She was a 42-year-old woman (gesta 4, para 3) with past medical history of depression treated with selective serotonin reuptake inhibitor and tobacco abuse. This last pregnancy was uneventful and delivery occurred by elective cesarean outside our institution. Twenty five days after delivery, she is admitted on our emergency department with dyspnea. Lung sounds were decreased on both pulmonary bases and peripheral saturation was 94% with 2 liters of oxygen. There were no alterations on cardiac auscultation. Electrocardiogram showed sinus rhythm and inverted T waves on V1-V6. Blood testing was normal apart from elevated pro-b-type natriuretic peptide levels. On thoracic computed tomography angiography, bilateral pleural effusion with diffuse ground-glass opacities were seen and pulmonary thromboembolism was excluded. Echocardiogram revealed moderately dilated left cavities with left ventricular ejection fraction (LVEF) of 35% with global hypokinesia and also right ventricle dysfunction. Coronary angiography excluded coronary artery disease. Cardiac magnetic resonance imaging excluded myocarditis. Therefore, PPCM was the most probable diagnosis and treatment for heart failure, anticoagulation and bromocriptine were initiated. The patient substantially improved and was discharged from the hospital six days later, on class II-III of the New York Heart Association (NYHA) classification. On six months reevaluation, she was on NYHA class II, with a LVEF of 40% and normal right ventricle function – class II NYHA. **Conclusion:** PPCM is a serious condition with considerable morbimortality. A high level of suspicion is required since timely diagnosis and treatment are crucial to optimize outcomes. *No conflict of interest to declare.*

## SEQUENTIAL INSTRUMENTATION IN OPERATIVE VAGINAL DELIVERIES – ARE THE RISKS OF MATERNAL AND NEONATAL MORBIDITY TOO HIGH?

Elizabeth O'Donnell, Margaret Pikovsky, Asad Rahim  
Obstetrics & Gynaecology Department, Imperial College NHS Trust, London, UK

**Problem statement:** The use of sequential instrumentation when performing operative vaginal deliveries (OVD) has been recognised to carry a higher risk of maternal and fetal morbidity compared with single instrument use 1. These risks can be higher than the sum of the relative risks of each individual instrument 2. For this reason, the RCOG recommends avoiding sequential instrumental use where possible 3. The alternative to sequential instrument use is 2nd stage caesarean section (CS) which is not without risk, carrying increased risk of massive obstetric haemorrhage compared to completed assisted delivery 4. **Methods:** We assessed neonatal and maternal outcomes of single vs. sequential instrumentation in a multicentre, retrospective

cohort study of women who underwent an OVD within two inner city maternity units. Term (37 weeks' gestation), cephalic, singleton pregnancies were included over a study period of 3 months. Primary outcome measures included 5-minute Apgar scores, paired cord gases, fetal injury, SCBU admission and maternal blood loss. **Results:** 300 OVDs occurred between two sites over the study period of which 285 met inclusion criteria; 24 used sequential instruments (8.9%). The first instrument used was metal cup ventouse (12/24) and Kiwi® Omnicup (12/24). The second instrument in all cases was Neville-Barnes forceps. There were 2 accounts (8.3%) of failed sequential instrumental resulting in conversion to 2nd stage CS. Comparison of outcomes between single and sequential instrumentation revealed no statistically significant differences in paired pH7.20 (OR 1, 0.1-8.2 p=0.65), neonatal Apgars 7 at 5 mins (OR 1, 0.98-1.04, p=0.9), SCBU admission (OR 2.2, 0.5-10.6, p=0.32) or fetal injury (OR 1.5, 0.2-12.8 p=0.052). However, maternal blood loss was higher and more likely to be over 1 litre in the sequential instrument group (OR 1.7, 1.1-4.3, p0.05). **Conclusion:** We observed no differences in neonatal outcomes with sequential instrument use compared to single instrument, however there was an increased risk of maternal blood loss. This may be because sequential instrument increases duration of delivery time and they are more likely to be used in mid-pelvic deliveries requiring fetal head rotation. Therefore, the decision to apply a second instrument must be judiciously balanced alongside the risks of a 2nd stage CS.

## FETAL VENTRICULOMEGALY: SHOULD SAME INVESTIGATION BE OFFERED IN ALL CASES?

Rodrigo Pereira Mata<sup>1</sup>, Monica Melo<sup>2</sup>, Catia Lourenco<sup>2</sup>, Francisco Valente<sup>2</sup>

<sup>1</sup>Gynecology/Obstetrics, Centro Hospitalar Universitario do Algarve, Portimao, Portugal

<sup>2</sup>Prenatal Diagnosis Center, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

**Problem statement:** Ventriculomegaly (VM) is defined as an enlargement of the atrium of the lateral ventricle <sup>3</sup> 10 mm. This finding is variably associated with chromosomal abnormalities, fetal infections and other malformations. Most literature, define a measurement of 10-12 mm as mild VM and considers an isolated VM in the absence of other apparent anomalies. Some authors manage mild isolated VM as a variant of the norm, therefore questioning benefit of additional investigations - magnetic resonance imaging (MRI), genetic and infection study - in all cases of VM. **Methods:** We conducted a retrospective continuous cohort study, including all cases of fetal VM managed in our prenatal diagnosis centre, between 2010 and 2019. Two groups were defined: group A (mild, isolated VM) and group B (moderate/severe or associated with other malformations). We compared main fetal characteristics, additional investigation results and pregnancy outcome in order to evaluate the pertinence of the medical workup offered and its importance in pregnancy course. Significance threshold was defined as a p-value 0.05. **Results:** 60 patients were included, with mean age of 30,6 (± 6,2) years-old. Mild, moderate and severe VM was reported in 47 (71,2%), 3 (5,1%) and 9 (15,3%) cases; in 23 (30,3%) cases there were associated malformations, the most frequent corpus callosum agenesis (n=5). VM was more common in male fetus (63,2%), in both groups. In group A, unilateral VM was significantly more common (71,4 vs 28,6%, p=0.001) and there were no cases of fetal infection or genetic abnormalities. The benefit of MRI was higher in group B (30 vs 3%, p=0.05). In group A, most of the fetus had spontaneous resolution of VM (77,1 vs 22,9%, p=0.001) with no cases of medical pregnancy termination or intra uterine death. **Conclusions:** Our results are according to the literature that face mild isolated VM as a benign situation, in what concerns pregnancy evolution and

outcomes. Ultrasound surveillance should be the rule in all cases. Although, protocol additional investigations (mainly MRI) should be considered dispensable in cases of mild, isolated and unilateral VM.

### MCDA PREGNANCY – NEC AS A CONSEQUENCE OF TTTS

**Ines Reis**, Patricia Ferreira, Carolina Carneiro, Carla Pina, Isabel Sa  
*Obstetrics, CHEDV, Porto, Portugal*

**Introduction** :TTTS is characterized by relative hypovolemia of one twin and hypervolemia of the other as a result of many or large arterio-venous anastomoses in the placenta. It occurs in 8 to 10% of twin pregnancies with monochorionic diamniotic (MCDA) placentation. Even with laser treatment, TTTS is associated with a perinatal mortality rate of 30-50%, and a 10% chance of long-term handicap, mostly neurological and renal but although less frequently, gastrointestinal ischemic lesions are also described. **Case Report**: A stage III TTTS was diagnosed on a 39 years-old, nuliparous healthy woman, with a MCDA diagnosed at 12 weeks. At 16+4 weeks, US showed fetus 1 with absent bladder and fetus 2 with augmented amniotic fluid, DV with inverted a-wave and tricuspid regurgitation. Laser photocoagulation of communicating vessels was performed at 16+6 weeks. One week after the procedure, both fetuses had normal amniotic fluid volume and Doppler. Following US were normal. At 35+4 weeks spontaneous labor occurred with a forceps extraction for fetus 1 (2230g, AI 6/8/8) and cesarean delivery of fetus 2 due rotation to transverse situation (2250g, AI 6/6/7). On the 3rd day after being admitted to the NICU, newborn 1 presented an hematic defecation. An abdominal X-ray confirmed neonatal necrotizing enterocolitis (NEC). Antibiotic therapy was initiated and he was transferred to a pediatric surgery department. On the 9th day, due to hemodynamic instability, a laparotomy was performed with ileocecal resection and terminal ileostomy. On the 46th day of life, the ileocolic anastomosis was performed. He was discharged on the 62nd day of life. Newborn 2 had an early respiratory distress syndrome and was discharged from the NICU on the 21st day of life, with no major complications. At 4 months of age newborn 1 weights 5430g and newborn 2 weights 5800g, both with normal motor and neurological development. **Conclusion**: 10% of NEC occurs in term infants related to intestinal malperfusion, and it can occur early in pregnancy as consequence of TTTS and its treatment. This case highlights the importance of US and the impact of laser treatment on TTTS although some complications cannot have prenatal diagnosis.

### CORRECTION OF THE IRON CONTENT IN THE BODY OF WOMEN AT THE STAGE OF PREPARATION FOR PREGNANCY

**Iryna Rudenko**, Valentyna Mishchenko, Anna Lavrinenko  
*Department of Obstetrics and Gynecology, Odessa National Medical University, Odessa, Ukraine*

**Formulation of the problem**: The aim of the study is to supplement the etiopathogenetic approaches to preventing the occurrence of obstetric-perinatal complications by using personalized preventive methods for correcting iron metabolism and substances that affect its metabolism, hereditary predisposition at the stage of preparation for pregnancy and by trimesters of gestation. **Methods**: 90 women of reproductive age at the stage of preconception preparation and pregnancy were examined. The content of iron, ferritin, folic acid, cyanocobalamin, alleles of folate cycle enzyme genes in the blood of women was determined before and during pregnancy. A pathogenetically substantiated personified algorithm has been developed for the prevention of obstetric-perinatal complications.

**Received results**: In the trimesters of pregnancy, the content of iron, ferritin, folic acid, cyanocobalamin in women who underwent preconception training in relation to the comparison control group was significantly higher ( $p < 0.001$ ). The frequency of polymorphic alleles of folate cycle enzyme genes was more than 70% in women of both groups. The decrease in the content of ferritin in the blood of women of the comparison control group was consistent with a decrease in the levels of iron, folic acid, and cyanocobalamin. In women who underwent the proposed preparation for pregnancy and preventive measures during gestational periods, the frequency and severity of anemia of pregnant women and other gestational complications was significantly lower than in the comparison group during three trimesters and the postpartum period ( $p < 0.05$ ).

**Conclusions**: The determination of the iron content and substances (ferritin, folic acid, cyanocobalamin) that affect its metabolism, at the stage of personified, staged preconception preparation 3-4 months before fertilization and gestational trimesters, is pathogenetically substantiated in order to prevent obstetric-perinatal complications, given the role of iron in metabolic processes, namely tissue respiration. The content of ferritin below or at the lower boundary of the reference values is a preclinical laboratory-confirmed risk factor for gestational and perinatal complications, which pathogenetically confirms the advisability of prescribing nutrient therapy, preparations of ferrous iron and vitamin metapholine complexes, especially in "carriers" of polymorphic alleles of folate cycle enzyme genes, which helps prevent obstetric and perinatal complications.

### AUTOIMMUNE HEMOLYTIC ANEMIA IN PREGNANCY AND A RARE COMPLICATION OF ITS MANAGEMENT: A CASE REPORT

**Raphael Santos**

*Department of Obstetrics and Gynecology, University of Santo Tomas Hospital, Manila, Philippines*

This is a case of a 24-year-old, Filipino, primigravid presenting with easy fatigability at 8 weeks AOG. She was initially seen by a general obstetrician and started on folic acid 5 mg once a day. CBC showed severe anemia (Hemoglobin 54 g/dL). On further work ups, liver enzymes and coagulation assays were normal. LDH, bilirubin and reticulocyte count were elevated. Peripheral blood smear showed normocytic hypochromic RBC. Direct Coombs test was positive however ANA was equivocal. At 11-12 weeks AOG, she was referred to our institution where she was transfused with a total of 3 units pRBC and received three cycles of methylprednisolone pulse therapy. Anti-dsDNA, lupus anticoagulant, anti-cardiolipin and b2 glycoprotein antibody were all negative. Complement factor 3 and serum 25-hydroxy vitamin D were within normal range. Assessment was autoimmune hemolytic anemia. She was started on prednisone 50 mg once a day. Serial monitoring of CBC was normal with no recurrence of anemia. At 27-28 weeks AOG, she developed GDM and was started on diabetic diet. 7-point CBG monitoring showed good glucose control. Congenital anomaly scan was unremarkable and steroid therapy was continued. At 34-35 weeks AOG, BPS showed oligohydramnios (AFI 2.15 cm). Despite adequate IVF hydration, repeat BPS showed persistent oligohydramnios (AFI 3.34 cm). She underwent primary LTCS and delivered to a live, late preterm male, BW 2.1 kg, AS 8,9. On physical examination, her baby had sacral dimpling. An ultrasound of the lumbosacral spine confirmed mild spina bifida. On her 2<sup>nd</sup> post-operative day, she developed persistent, throbbing bitemporal headache accompanied by nausea and photophobia which was unrelieved by acetaminophen and NSAIDs. Cranial MRI revealed a multiloculated brain abscess. On further history taking, patient disclosed history of dental caries since May 2019. She underwent right temporal craniotomy for

evacuation of the brain abscess which on culture showed growth of *Nocardia* spp. She was started on Imipenem 500 mg/IV infusion every 6 hours and Trimethoprim-Cotrimoxazole 160/800 mg/tab 2 tablets every 8 hours for two weeks. Patient drastically improved and serial CBC were normal with no recurrence of anemia. Repeat Coombs test was negative 6 weeks post-caesarean section.

#### PLACENTAL INDEX, PLACENTAL CHARACTERISTICS, BIRTHWEIGHT, AND NEONATAL OUTCOME IN PREGNANCIES

**Leo Simanjuntak**, Patrick Anando Simanjuntak  
*Obstetrics and Gynecology Department, Faculty of Medicine, Universitas HKBP Nommensen, Medan, Indonesia*

**Problem Statement:** Placental anatomy, physiology, and molecular structure remain some of the most intriguing and understudied topics in obstetrics. Recent studies have highlighted the clinical importance of placental weight, as predictors of maternal, perinatal, and neonatal morbidity and mortality. The placental index is defined as the ratio between placental weight and the fetal weight. Placental index is often considered as an placental efficiency indicator. The objective of this study is to describe and determine correlation of placental index with pregnancy and neonatal outcome. **Methods:** This study used a cross-sectional design using primary data obtained from Mitra Sejati, Herna, and Methodist Sussana Wesley Hospital in Medan, Indonesia, for all women delivering singleton term pregnancy in Medan from January to August 2020. 431 consecutive single term pregnancies included in this study. **Results:** Mean newborn weight  $3246.36 \pm 484.87$  gram (range 1170 – 4800 gram). Mean placental weight was  $594.78 \pm 94.85$  gram (range 300-900 gram). Mean placental-fetal weight ratio was  $0.18 \pm 0.02$  (range 0.12 – 0.30). There were no significant mean placental-fetal weight ratio difference between male ( $0.184 \pm 0.00$ ) and female ( $0.186 \pm 0.00$ ) infants, primigravida ( $0.184 \pm 0.03$ ) and multigravida ( $0.186 \pm 0.03$ ), and umbilical cord insertion group ( $p > 0.05$ ). There was no significant correlation between placental index and Apgar score at 1 and 5 minute. There was a significant positive correlation between birth weight and placental weight ( $r = 0.52$ ) and there was a significant and progressive placental index decrease in birth weight group ( $p > 0.05$ ). **Conclusions:** There was no mean placental index difference in gender, parity, and umbilical cord insertion group. There was no significant correlation between placental index and Apgar score at 1 and 5 minute. There was a significant positive correlation between birth weight and placental weight and a significant and progressive placental index decrease in birth weight group.

#### ANXIETY LEVELS AND RELATED FACTORS IN TERM PREGNANT WOMEN UNDERGOING CAESAREAN SECTION

**Patrick Anando Simanjuntak**, Leo Simanjuntak  
*Obstetrics and Gynecology Department, Faculty of Medicine, Universitas HKBP Nommensen, Medan, Indonesia*

**Problem Statement:** In pregnancy biochemical factors and stressors can affect mental health, especially during perinatal. Anxiety is the most common psychiatric disorders in pregnancy. Anxiety in pregnancy is related to preterm labor, fetal growth restriction, and poor neurobehavioral development. Specifically, anxiety before cesarean section can increase anesthesia use during surgery, the need for postoperative analgesics, and causing an immunocompromised condition. This study aimed to assess the maternal anxiety level and related factors on caesarean section. **Methods:** This is a cross-sectional study using primary data of outpatient visiting private maternity clinic on April-May 2020. Based on defined criteria, 117 subjects were recruited in this study. Anxiety

level assessed using Hamilton Anxiety Rating Scale (HAM-A). Demographic data collected using research questionnaire. Logistic regression was used to identify associated factors on anxiety level. **Results:** Mean subjects age was  $29.44 \pm 5.90$  years. Mean HAM-A score was  $9.90 \pm 5.80$  point. Three components that contribute the highest score to the total score was anxious mood component ( $1.56 \pm 0.74$  point), insomnia (sleep disturbance) component ( $1.40 \pm 0.67$ ), and tension component ( $1.38 \pm 0.73$ ). Based on parity level, 35 women (29.9%) was primiparous and 82 women (70.1%) was multiparous. The results showed majority of the pregnant women (76.9%) showed no anxiety in undergoing caesarean section. The rest of these pregnant women (23.1%) showed mild anxiety level (13.7%) and moderate anxiety (9.4%). Majority of the pregnant women (56.4%) have had caesarean section before. There was no statistically significant correlation between age, education background, income level, parity level, occupation, and history of caesarean section, meaning the anxiety level was not affected by these associated factors ( $p > 0.05$ ). **Conclusions:** Majority of the pregnant women showed no anxiety in undergoing caesarean section. The anxiety level was not affected by age, education background, income level, parity level, occupation, and history of caesarean section factors. Family support, informative and educative advices and suggestions of caesarean section to pregnant women can make pregnant women not worried about caesarean section. **Keywords:** Anxiety; Pregnant Women; Caesarean section; HAM-A

#### PERIPARTUM CARDIOMYOPATHY: A CASE REPORT

**Catarina Soares<sup>1</sup>**, Sara Coelho<sup>2</sup>, Filipa Nunes<sup>1</sup>, Jorge Ribeiro<sup>1</sup>

<sup>1</sup>*Obstetrics and Gynaecology Department, Centro Hospitalar Do Oeste, Caldas Da Rainha, Portugal*

<sup>2</sup>*Obstetrics and Gynaecology Department, Centro Hospitalar Lisboa Central - Maternidade Dr. Alfredo da Costa, Lisboa, Portugal*

**Problem statement:** Peripartum cardiomyopathy (PPCM) is a rare cause of heart failure (HF), occurring in the last month of pregnancy or in the first five months postpartum in absence of known cause or pre-existing heart disease. It is considered a multifactorial disorder. The principal hypotheses with regards to its pathogenesis include autoimmune response, abnormal reaction to physiologic hormones or a viral aetiology. Risk factors include multiparity, advanced maternal age, multiple pregnancies, pre-eclampsia, chronic hypertension, smoking, alcoholism, malnutrition and long-term tocolysis. The diagnosis of PPCM is made in the presence of symptoms and signs of HF, ventricular systolic dysfunction and after excluding other possible causes. **Methods:** Literature review and retrospective analysis of a case of peripartum cardiomyopathy. **Results:** A 34-year-old primigravida with history of chronic hypertension and gestational diabetes was admitted to the obstetric department at 37 weeks of pregnancy due to pre-eclampsia. She was treated with magnesium sulfate and intravenous antihypertensive drugs. An urgent caesarean section was performed due to fetal distress, delivering a girl of 2555g and Apgar score of 4/9/10. The next day, the mother developed severe dyspnoea, hypertension (181/118mmHg) and psychomotor disorientation. Arterial gasometry revealed mixed acidosis. Electrocardiography showed sinus rhythm and left ventricular hypertrophy criteria. Computed tomography scan excluded pulmonary embolism and revealed pleural effusion and discrete cardiomegaly. Echocardiographic examination was consistent with left ventricular dysfunction. There was no evidence of coronary artery disease. TnT level were at 25.9ng/l and NT-pro-BNP level at 854pg/mL. Due to deterioration of her condition, she was intubated, transferred to the intensive care unit and treated with heart failure medication and inotropes, which stabilised her condition. On day 2 she was extubated. After 14 days, she

was asymptomatic with ventricular function fully recovered and had hospital discharge. **Conclusion:** PPCM represents a life-threatening, yet underdiagnosed disease seriously affecting young women. There is a considerable overlap with other conditions, so the differential diagnosis may be a challenge. When promptly identified and correctly treated, the overall prognosis is favourable.

#### ANALYSIS OF LEPTIN CONCENTRATION IN THE BLOOD SERUM OF WOMEN GIVING BIRTH AND IN THE UMBILICAL BLOOD FROM PROPERLY DEVELOPING PREGNANCIES AND PREGNANCIES WITH SELECTED COMPLICATIONS

**Malgorzata Stefaniak**, Ewa Dmoch-Gajzlerska

Faculty of Health Sciences, Department of Obstetrics and Gynecology Didactics, Medical University of Warsaw, Warsaw, Poland

**Problem statement:** Studies on leptin indicate its role in the physiology and pathophysiology of pregnancy. It is suggested that leptin may be a prognostic marker for some complications during pregnancy. **Methods:** The research encompassed a group of 379 women. The control group consisted of 194 health women in physiologically pregnancy. Research group consisted of 185 pregnant women including 61 women with gestational diabetes mellitus, 39 with hypothyreosis, 36 with pregnancy induced hypertension, 25 with a diagnosis of intrauterine growth restriction and 24 with pregnancy-related intrahepatic cholestasis. The sample material gathered for leptin concentration analysis consisted of two independent components: fetus- and placenta-derived material. The analysis was performed using ELISA. **Results:** Average leptin concentration in the blood of women giving birth after a physiologically-standard pregnancy was 37,17 ng/ml ( $\pm 28,07$ ). Reference range (33,19-41,14 ng/ml). Average leptin concentration in the umbilical blood from physiologically-standard pregnancy was 14,78 ng/ml ( $\pm 15,97$ ). Reference range (12,52-17,04 ng/ml). The group of pregnant women with pregnancy-induced hypertension was observed to have significantly higher leptin concentration (61,04 ng/ml ( $\pm 28,07$ )) than the healthy control group. Average leptin concentration in the umbilical blood in the same group was 24,02 ng/ml ( $\pm 27,98$ ). Significantly higher leptin concentrations were detected in the blood of women in pregnancies complicated by diabetes (48,65 ng/ml  $\pm 35,44$ ), hypothyreosis (48,13 ng/ml  $\pm 31,09$ ), or intrauterine growth restriction (52,73 ng/ml  $\pm 30,49$ ). No statistically significant difference in leptin concentration levels was detected between physiologically standard pregnancies and pregnancies affected by intrahepatic cholestasis. In diabetes-affected pregnancies significantly higher leptin concentrations in the umbilical blood were observed (26,67 ng/ml  $\pm 27,98$ ). In the case of pregnancies affected by intrauterine growth restriction the average concentration was significantly lower (7,97 ng/ml  $\pm 4,46$ ) in comparison with the average for physiologically standard pregnancies. The research detected no statistically significant difference between leptin concentration levels in pregnancies affected by pregnancy-related intrahepatic cholestasis and those affected by hypothyreosis. **Conclusions:** The research points to differences in leptin concentration having predictive value in diagnosis of some pregnancy-complicating conditions, although there is a need for further research into the matter.

#### TELEMETRIC INTERVENTIONS IN THE MANAGEMENT OF WOMEN WITH GESTATIONAL DIABETES MELLITUS

**Claudia Eberle, Stefanie Stichling**

Medicine, Hochschule Fulda - University of Applied Sciences, Fulda, Germany

**Problem statement:** Gestational diabetes mellitus (GDM) is a major clinical health problem. One of six births was affected by GDM in 2019 and about 16% of live births had some form of hyperglycemia. GDM is associated with short and longterm consequences for mother (e.g. pre-eclampsia, metabolic syndrome, coronary heart disease) and offspring (e.g. macrosomia, obesity, type 2 diabetes). Innovative strategies are required to improve the clinical management of GDM. Telemetry provides new digital opportunities. We aimed to review the evidence regarding the clinical effectiveness of telemetric interventions in the management of GDM. **Methods:** We conducted a systematic meta-review searching MEDLINE (PubMed), Web of Science Core Collection, EMBASE, Cochrane Library, and CINAHL databases for randomized controlled trials, systematic reviews, meta-analyses, and clinical trials published from January 2008 to April 2020. Reference lists were searched manually. Study quality was assessed using "A MeaSurement Tool to Assess systematic Reviews" (AMSTAR 2) and "Effective Public Health Practice Project" (EPHPP). Interventions were classified regarding communication channels between patients and health care professionals. **Results:** From  $n=1116$  unique citations,  $n=8$  studies were included ( $n=474$  patients;  $n=2177$  patient cases):  $n=3$  systematic reviews / meta-analyses ( $n=1$  high,  $n=2$  moderate quality),  $n=4$  randomized controlled trials ( $n=1$  high,  $n=3$  moderate quality) and  $n=1$  low quality non-randomized controlled trial. We classified  $n=3$  "asynchronous" internet / web-based and  $n=2$  "asynchronous and synchronous" internet / web-based and telephonically interventions. 1-h and 2-h postprandial blood glucose levels showed slight improvements in a moderate quality meta-analysis mean difference (MD) -0.02% (95% CI -0.36 to 0.32)  $P=0.39$ . Fasting blood sugar and mean glucose were lower in intervention groups, not significant, but two-thirds of intervention subjects achieved mean glucose level of  $<110$  mg / dL in one study. Neonatal hypoglycaemia showed improving trends. Nursing interventions increased by about 10-fold (10.3 vs. 0.9,  $P<0.001$ ) in intervention group (by e-mails and phone calls). Improvements in empowerment were reported. **Conclusion:** Telemetric interventions indicated improving tendencies in better glycemic control and in maternal and neonatal outcomes in general by enabling closer management of GDM patients. More studies are required.

#### NOVEL INSIGHTS IN GESTATIONAL DIABETES MELLITUS CARE BY APPROACHING MOBILE HEALTH APPLICATIONS (MHEALTH-APPS)

**Maxine Loehnert, Claudia Eberle, Stefanie Stichling**

Medicine, Hochschule Fulda - University of Applied Sciences, Fulda, Germany

**Problem statement:** Gestational diabetes mellitus (GDM) emerges worldwide with increasing prevalence and is closely associated with adverse short and long-term outcomes in women and their offspring, such as pregnancy and birth complications respectively comorbidities, type 2 diabetes, metabolic syndrome as well as cardiovascular disease. Against this background, mobile health applications (mHealth-Apps) do open up new possibilities to improve the management of GDM. Therefore, we systematically reviewed studies that evaluated diabetes specific mHealth-Apps in GDM care compared to control groups. **Methods:** MEDLINE (PubMed), Cochrane Library, Embase, CINAHL and Web of Science Core Collection databases were systematically searched. An additional manual search in references and Google Scholar was performed. We included controlled clinical trials published from 2008 to 2020. Study quality was assessed using the "Effective Public Health Practice Project" (EPHPP) tool. Study results were categorized by outcomes. **Results:** From  $n=114$  citations,  $n=6$  publications, analyzing  $n=408$  GDM patients in the intervention and  $n=405$  in the control

groups, were included (n=4 moderate and n=2 weak quality). Of these, n=5 were two-arm randomized controlled trials (RCT) and n=1 controlled clinical trial (CCT). Findings indicate that patients were highly satisfied with mHealth-Apps in GDM care. Intervention subjects agreed that Apps made them more engaged in health (P0.01). The quality of the treatment improved by closer monitoring and time saving. In one study, frequency of outpatient service was significantly lower in the intervention group (P0.001). One study showed lower costs per delivery, mean cost difference -£1044 (95% CI -£2186 to £99). **Conclusion:** mHealth-Apps improve the quality of life in GDM care and offer a highly promising approach in the field of digital diabetology. Since the evidence is limited, further studies are necessary.

### POOR SLEEP IS ASSOCIATED WITH HIGHER BLOOD PRESSURE IN PREGNANCY AND HIGHER UTERINE ARTERY PULSATILITY INDEX

**Yafang Tang**, Jun Zhang, Fei Dai, Nurul Syaza Razali, Shephali Tagore, Bernard SM Chern, Kok Hian Tan  
*Obstetrics and Gynecology, KK Women's and Children's Hospital, Singapore*

**Problem statement:** Sleep disturbances have been recognized as a significant complication during pregnancy which can give rise to adverse maternal and fetal outcomes. Studies had shown that sleep disturbances are associated with pre-eclampsia and pregnancy induced hypertension. There has been no systemic study on sleep disturbances' correlation with blood pressure during pregnancy. We aim to elucidate the correlation between sleep disturbances and blood pressure during pregnancy in women with no pre-existing hypertension in a prospective cohort study.

**Methods:** A total of 926 subjects were recruited in the outpatient specialist clinics at KK Women's and Children's Hospital, Singapore, between September 1, 2010, and August 31, 2014. Our study is a prospective cohort study.

**Results:** Our study showed that sleep progressively worsened as pregnancy advanced. Poorer sleep efficiency and shorter sleep duration were associated with higher blood pressure, especially in the first trimester. Mixed model analysis showed overall positive association between sleep quality (using PSQI score) with diastolic blood pressure (DBP) (p0.001) and mean arterial pressure (MAP) (p=0.005) for all trimesters. Sleep duration was found to be negatively associated with both systolic blood pressure (SBP) (p=0.029) and DBP (p=0.002). Overall poor sleep during pregnancy was also associated with higher uterine artery pulsatility index. **Conclusion:** Our study demonstrated that sleep quality is significantly associated with blood pressure during pregnancy with most prominent effect in the first trimester. Poor sleep quality is also associated with higher uterine artery PI.

### INCIDENCE OF MYCOPLASMA HOMINIS, UREAPLASMA UREALYTICUM AND PREGNANCY OUTCOME

**Ilir Tasha<sup>5</sup>, Daniela Tasha<sup>1</sup>, Nikita Manoku<sup>2,4</sup>, Artan Simaku<sup>3</sup>**

<sup>1</sup>Faculty of Technical Medical Sciences, Medicine University, Tirana, Albania

<sup>2</sup>Obstetric Gynecology Department, Faculty of Medicine, Tirana, Albania

<sup>3</sup>Health Public Institute, Health Public Institute, Tirana, Albania

<sup>4</sup>Obstetric Gynecology Department, Obstetric Gynecology Albanian Association, Tirana, Albania

<sup>5</sup>Obstetric Gynecology Department, Private Clinic "Plus", Tirana, Albania

Mycoplasma hominis (M Hominis) and Ureaplasma urealyticum (U.urealyticum) are important opportunistic pathogens that cause urogenital infections and complicate pregnancy. The aim of this study was to investigate the

effects of them on pregnancy outcomes and antimicrobial susceptibilities of M. Hominis and U. Urealyticum.

**Methods:** We tested vaginal swabs obtained from 172 women for the presence of genital mycoplasmas between June 2015 and 2019 at Obstetric Gynecology University Hospital "Koco Gliozheni" and private obstetric Gynecology Clinic "PLUS" Tirana, Albania. Sociodemographic and clinical data of the women participating in the study were collected through an individual file. **Results:** 132(76,7%) of women were pregnant with a mean gestational age 25,5(+/-4,9)weeks range 14-35 weeks. The incidence of M hominis was 5,8%, of U urealyticum 22,7%, of Mh+&Uu+(46,5%), of Mh+&Uu+ plus Polimicrobial infection was 21,5%, of Mh-&Uu+ plus polimicrobial infection 10.5% and of Mh-&Uu+ plus non Polimicrobial infection was 12,2%.PPROM occurred in 14(10,6%) of pregnant women, premature birth in 31(23,5%) and birth in term in 100(75,8%) of them. The relative risk for preterm birth was 6 times higher among women with Mh+&Uu+ plus polimicrobial infection(RR=6.0 (5% CI3. 18-11.31p,0.001) and 4.4 times higher(RR=4,495%CI 1,78-11,09 p=0,001) among women with Mh-&Uu+ plus Polimicrobial infection as compared to other women. In multivariate logistic regression model adjusted for clinical variables independent predictors of preterm birth were found Mh+&Uu+ plus Polimicrobial infection(p0,001), gestational age(p=0.001) and number of abortions (p=0.04). (2,2 % of women with M hominis and (94,1%) of them with U urealyticum were treated with antibiotics. **Conclusion:** The incidence of M hominis and /or U urealyticum infections in pregnant women were high. Therefore, to maintain a safe pregnancy, it is important to identify them and to use appropriate antibiotics immediately

**Key words:** M hominis, U Urealyticum, PPROM, preterm birth, treatment

### NIPT VERSUS AMNIOCENTESIS IN FIRST TRIMESTER SCREENING FOR CHROMOSOMAL ABNORMALITIES IN PATIENTS WITH HIGH RISK OF TRISOMY 21,18 AND INTERMEDIATE-RISK OF TRISOMY 21

**Ilir Tasha<sup>1</sup>, Daniela Tasha<sup>2,3</sup>**

<sup>1</sup>Obstetric Gynecology, Obstetric Gynecology University Hospital "Koco Gliozheni", Tirana, Albania

<sup>2</sup>Obstetric Gynecology, Faculty of Technical Medical Sciences, Tirana, Albania

<sup>3</sup>Obstetric Gynecology, University of Medicine, Tirana, Albania

Screening and diagnosis of chromosomal abnormalities still remain the cornerstone not only for genetic prenatal diagnosis but also for the future of the society. Almost all pregnant women in Albania are offered the first trimester combined screening test (FTCST) from 11 - 13 weeks plus 6 days in related to Downs", Edwards" and Patau"s syndromes. FTCST includes ( maternal age, Fetal heart rate, nuchal translucency NT, FREE beta-HCG, PAPP\_A serum level) can identify 90% of fetuses with trisomy 21 and other major chromosomal abnormalities for a false positive rate of 5%. CVS and Amniocentesis are not feasible options for all low-risk mothers, as they carry out a small but finite risk of miscarriages. We have to encourage the Ob/GYN to use NIPT in the screening of the chromosomal abnormalities in patients classified as high risk and intermediate risk based on the results of the FTCST. Methodology prospect study. Assessment of the correlation between FTCST, NIPT results with amniocentesis answers from November 2015 - January 2020. **Results:** 300 patients underwent FTCST with the following results: 120 cases with a high risk of trisomy 21 and 18 plus 60 with an intermediate risk of trisomy 21. 150 out of 180 underwent NIPT testing and 30 patients with intermediate risk did not accept. From 120 cases with High risk of trisomy 21 and 18 based on FTCST - 5 resulted in NIPT positive for trisomy 21 and 1 for trisomy 18, meanwhile, 2 out of 30 cases of intermediate-risk subgroup resulted in NIPT positive for trisomy 21. One case NIPT positive for trisomy 21 lost to follow up. All NIPT positive for trisomies 21 and 18 underwent the

amniocentesis, which did confirm the same result as NIPT testing. **Instead of conclusion:** We must not push the patients with low risk of trisomies 21, 18, and them with an intermediate risk of trisomy 21 selected by the first trimester combined screening test FTCST to choose amniocentesis before the NIPT testing.

#### FETOPLACENTAL MOSAICISM AND NON-INVASIVE PROCEDURE TESTING (CASE STUDY)

Ilir Tasha<sup>1</sup>, Daniela Tasha<sup>2</sup>, Erlind Kurti<sup>3</sup>, Arjan Alikaj<sup>1</sup>, Robert Luto<sup>4</sup>

<sup>1</sup>Obstetric Gynecology, Ob/gyn University Hospital Koco Gliozheni, Tirana, Albania

<sup>2</sup>Obstetric Gynecology, Faculty of Technical Medical Sciences, Tirana, Albania

<sup>3</sup>Obstetric Gynecology, Ob/gyn University Hospital "Mbretresha Geraldine", Tirana, Albania

<sup>4</sup>Obstetric Gynecology, Spitali Rajonal Fier, Fier, Albania

Prenatal diagnosis is now part of established obstetric practice in many countries especially non-invasive procedure diagnosis by using free nucleic acids in maternal plasma. As with all screening tests, false positive (FP) and false-negative(FN) results may occur. This is due to fetoplacental mosaicism- a biological phenomenon that resulted from the presence of cells with different genetic compositions in the same individual. it usually occurs during the process of mitotic cell division. Mosaicism can be an underlying biological cause of discordant. Methods: we enrolled in our study 70 cases who had different indications of using the NIPT.66 cases resulted NIPT negative. All of them delivered normal babies. 4 out of 70 cases resulted in respectively 2 with trisomies 21; one trisomy 18, which are confirmed by amniocentesis. Only one case with abnormal sonographic finding (atrioventricular canal), femur length. **Instead of conclusion:** Despite exciting advances, underlying biologic mechanisms will allow neither sensitivity nor specificity of 100 % percent.

#### UREAPLASMA UREALYTICUM AND MYCOPLASMA HOMINIS AMONG PREGNANT WOMEN

Daniela Tasha<sup>1</sup>, Ilir Tasha<sup>2</sup>

<sup>1</sup>Obstetric Gynecology, Faculty of Technical Medical Sciences, Tirana, Albania

<sup>2</sup>Obstetric Gynecology, Ob/gyn University Hospital Koco Gliozheni, Tirana, Albania

**Introduction:** Genital mycoplasmas, including M. hominis and U. urealyticum contribute to some of the reproductive health pathologies and pose a significant public health problem associated with preterm birth, miscarriage, stillbirth and low birth weight.

**Aim:** the aim of the study was the evaluation of the role of Mycoplasma Hominis and Ureaplasma Urealyticum in reproductive health. **Material and methods:** This is a prospective study conducted at the Department of Obstetrics and Gynecology, University Hospital "Koco Gliozheni", Tirana, Albania, in the period 2013-2019. This study included 172 pregnant and non-pregnant women. Sociodemographic and clinical data of women participating in the study were collected through an individual file.

**Results:** M. Hominis was found in 90 (52.3%) [95% CI 44.56 - 59.95] of total women while U. Urealyticum in 119 (69.2%) [95% CI 61.72 - 76.0] of them. Mycoplasmas have almost the same distribution according to age group, pregnancy status, parity, and the number of abortions. No significant difference was found in the distribution of MH (p = 0.8%) and UU (p = 0.2) according to the number of abortions. Mixed infection was found in 51 (26.7%) of women. The incidence of mixed infection was highest for MH + UU + (10.9%) followed by UU + (9.9%). In the multivariate logistic regression model, significant and independent factors of preterm birth risk resulted: U. Urealyticum (p0.01), Gestational age (p = 0.03) Mixed

mycoplasma (p0.001). (92.2%) of women with M. Hominis and (94.1%) of women with U. Urealyticum were treated with antibiotics. **Conclusion:** Organization of the screening programs for the infection by mycoplasmas to prevent premature birth and reduce the cost of its treatment. to maintain a safe pregnancy, it is important to identify the isolates and use the appropriate antibiotics immediately. **Keywords:** M. Hominis, U. Urealyticum, incidence, pregnancy, reproductive health

#### ASCENDANT INTRAUTERINE INFECTION OF CANDIDA ALBICANS IN THE PREGNANTS WITH SYPHILIS

Tetiana Yaremchuk

Department of Obstetrics, Gynaecology and Perinatology of the Faculty of PGE, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Obstetrical Department, Lviv Regional Clinical Perinatal Center, Lviv, Ukraine

**Problem statement:** Ascendant intrauterine infection of Candida albicans (CA) is detected in cases of perinatal complications and remains an unexplored and unclear pathology. Intrauterine candidiasis occurs without premature rupture of fetal membranes. Necrotizing funisitis and severe chorioamnionitis without villitis are the markers of intrauterine candidiasis. The development of multiple green or white abscesses on the umbilical cord surface is characteristic of intrauterine fungal infection. Abscesses with mycelium are located mainly on the surface of the umbilical cord, but the invasion in Wharton's jelly can also be observed. Mycelial invasion is a risk factor for hematogenic dissemination of candidiasis and fetal infection. The methods of research were clinical, CTG, USG, Doppler, microbiological, morphological, statistical methods. Microbiological researches were conducted by inoculation of media. Materials of research were 41 case records of pregnant women with early latent syphilis and 44 case records of healthy pregnant. Bacteriological examination of cervical and vaginal secretions was performed for 30 women before specific treatment and in term pregnancy, for 11 syphilitic women with antenatal fetus death, for 44 healthy pregnant in 2011-2016. **Results:** The uterine stage of ascendant intrauterine fungal infection with the presence of CA or CA-microbial associations in the cervix of uteri and vagina was revealed. CA has been determined in the cervix and vagina predominantly with Escherichia coli in all cases of antenatal fetus death in concentration 1\*10 in 6-7 degrees CFU/g. Lactobacilli spp. were absent. CA was discovered in 33,33+/-8,75 % of pregnant before treatment (as a monoculture in 30,0+/-15,3 %, in pathogenic concentrations together with Staphylococcus epidermidis or Lactobacilli spp. in 40,0+/-16,3%, in association with Escherichia coli in 30,0+/-15,3%). Some strains of CA were totally resistant to fungicides. CA was defined in 40,0+/-9,1 % of treated pregnant in concentration 1\*10 in 2-4 degrees CFU/g, whereas in healthy pregnant - in low concentrations only in the vagina in 6,82+/-3,84% of cases (P0,01). **Conclusion:** Severe vaginal dysbiosis was determined in the pregnant with syphilis. Ascendant intrauterine infection of Candida albicans or Candida albicans-microbial associations in the cervix of uteri and vagina were revealed. Pathomorphological signs of fetus and afterbirth fungal damage were absent.

#### BACTERIOPHAGES IN PREVENTION OF RECURRENT VAGINAL INFECTIONS FOR PREGNANT WOMEN

Tatiana Zefirova<sup>1</sup>, Alexander Zurabov<sup>2</sup>

<sup>1</sup>Obstetrics and Gynecology, Kazan State Medical Academy Branch Campus of the Federal State Budgetary Educational Institution of Further Professional Education Russian Medical Academy of Continuing Professional Education, Kazan, Russia

<sup>2</sup>Microbiology, Research and Production center "Micromir", Moscow, Russia

**Problem statement:** Female vaginal infections (aerobic vaginitis, vaginal candidiasis, bacterial vaginosis) among pregnant women may be recurring in 10-30% of cases, leading to the increased risk of complications for the mother and the fetus. Supporting the balance of the vaginal microbiota after treatment of the infectious condition is a reliable way to prevent relapses. Use of dedicated complex bacteriophage cocktails seem to be a natural ecologically friendly option. **Methods:** We observed 67 pregnant women with 3 or more episodes of vaginal infection during the first and second trimester. Each of them was randomly assigned to one of two groups. The main group included 34 women who were prescribed topical gel preparation Phagogyn immediately after local antibacterial therapy. The gel contains a complex of 64 bacteriophages with lytic activity against main opportunistic bacteria implicated in vaginal infections. The gel was applied as a care product up to the delivery. 33 patients in the control group were receiving standard local therapy in accordance with the clinical Protocol. The groups did not differ in age composition, parity, and nature of infectious processes. **Results:** In the main group, relapses of vaginal infection occurred in 4 cases (11.7%). In the comparison group, relapses requiring regular treatment were significantly more frequent - 21 cases, - 63.6% ( $x^2 = 20.6$ ,  $p0.0001$ ). Relapses in the main group never occurred more than once, in the comparison group the number ranged from 1 to 4, averaging  $1.90 (\pm 95\% \text{ CI } 1.52-2.28)$ . Inter-relapse interval was 79.25 days in the main group ( $SD 8.46$ ), against 31.04 days in the comparison group ( $SD 10.46$ ,  $t = 8.64$ ,  $p0.0001$ ). **Conclusion:** The use of complex bacteriophage cocktails designed specifically for vaginal microbiota contributes positively to the reduction of frequency of relapses among pregnant women and helps to lengthen intervals between relapses. This may be due to the stabilizing effect of bacteriophages on the bacterial community in the vaginal biotope. With ever expanding bacterial resistance to antibiotics, there is a growing demand for more ecological alternatives to handle infectious conditions, especially in sensitive patient groups.

#### EFFECT OF INTRAVENOUS IRON ON PERINATAL OUTCOMES IN PREGNANT WOMEN WITH ANEMIA

Tatiana Zeffirova<sup>1</sup>, Eugeny Yupatov<sup>1</sup>, Rozaliya Zamaleeva<sup>1</sup>, Renata Mukhametova<sup>2</sup>, Laysan Khaertdinova<sup>2</sup>

<sup>1</sup>Obstetrics and Gynecology, Kazan State Medical Academy, Kazan, Russia

<sup>2</sup>Obstetric, Kazan (Volga region) Federal University, Kazan, Russia

**Problem statement:** During pregnancy iron deficiency anemia may be resistant to oral iron medications. Intravenous iron therapy is more effective. But its effect on perinatal effects needs to be studied. **Methods:** We observed 79 pregnant women who had moderate or severe iron deficiency anemia. Due to the ineffective oral therapy, patients received intravenous carboxymaltose iron in dose of 1500 mg. The patients were divided into 2 groups. The first group included 40 women who received infusions at less than 32 weeks of pregnancy. In the second group (39 women), treatment was performed at 33-36 weeks of pregnancy. **Results:** As a result of intravenous iron treatment, hemoglobin levels increased equally in both groups. Before childbirth, it was  $103.17 \text{ g/l } (SD 5.11)$  in the first group and  $105.12 (SD 4.62)$  in the second group ( $t = 1.77$ ,  $p = 0.07$ ). It did not differ statistically, but the frequency of preterm birth tended to differ. It was 8.1% and 17.7%, respectively, in groups I and II ( $x^2 = 0.61$ ,  $p = 0.43$ ). However, some indicators of perinatal outcomes were different. The women in the second group had a large number of complications. In particular, the weakness of contractions was observed in 25.6%, but in 7.5% in the first group ( $x^2 = 4.7$ ,  $p = 0.03$ ). Fetal hypoxia of various degrees

at birth was detected in 30.7%, and in the first group only in 11.1% ( $x^2 = 5.8$ ,  $p = 0.016$ ). In addition, newborns from the second group had a smaller body weight. It was  $3079.4 \text{ g } (SD 240.5)$ , and in the first group -  $3241.2 \text{ g } (SD 224.1)$  ( $t = 3.09$ ,  $p = 0.002$ ). **Conclusion:** Intravenous iron carboxymaltosate is an effective medicament for the treatment of pregnant women anemia in cases where it does not respond to therapy with tablets. However, it seems rational to prescribe intravenous iron at an earlier stage, in particular in the second trimester or at the beginning of the third trimester. In these cases, not only increases the level of hemoglobin, but also improves perinatal outcomes. Apparently, later therapy cannot compensate for those pathological tissue processes that have already developed and are irreversible.

## GYNECOLOGICAL ONCOLOGY

### CERVICAL CANCER HPV NEGATIVE

Sara Bernardes Da Cunha<sup>1</sup>, Marta Pinto<sup>2</sup>, Sofia Raposo<sup>3</sup>, Rita Sousa<sup>3</sup>, Paulo Aldinhas<sup>3</sup>, Luis Sa<sup>3</sup>

<sup>1</sup>Gynecology and Obstetrics, Centro Hospitalar De Entre Douro E Vouga, Feira, Portugal

<sup>2</sup>Gynecology and Obstetrics, Centro Hospitalar De Baixo Vouga, Aveiro, Portugal

<sup>3</sup>Gyneaxology, Instituto Portugues De Oncologia De Coimbra, Coimbra, Portugal

**Problem statement:** Cervical cancer is the 6th most common cancer in women, with an incidence described in the order of 7,2/100.000 (1). High risk Human Papilloma Virus (Hr-HPV) infection persistence is one of the major causes for cervical cancer. In 99,7% of cases virus genetic material is detected (2-3). The objective of this work is to present a case report of cervical cancer with Hr-HPV test negative. **Methods: Case report description: Clinical case:** 56 years old women was sent to evaluation to an oncology center due to detection of a bleeding lesion of the cervix. Healthy and non-smoker, with 5 previous deliveries. Menopause occurred at age of 53, without any replacement hormonal therapy. The previous HPV test was 7 months earlier, with negative result. In the physical exam there were non vulvar lesions. At cervical exam there was a nodular lesion with vaginal invasion. It had 6-7 cm of major diameter. In the biopsy an epidermal carcinoma grade 1 was detected. Magnetic resonance image revealed a both parameters and vaginal involvement. Adenopathy were identified in both iliac chains, so a IIC cervical cancer was diagnosed. **Conclusion:** HPV infection is a primary cause of cervical cancer and its pre-malignant lesions. Cervical cancer screening is the main responsible for worldwide mortality reduction. HPV test is being pointed as an optimal screening test in prevention of invasive carcinoma, being 60-70% superior to pap smear, and with a negative predictive value near 100%. This clinical case focus on the possibility of missed diagnosis based only in HPV test, in advanced cervical cancer.

### GRANULOSA CELL TUMORS - TWO DISTINCT CLINICAL COURSES

Carolina Carneiro, Sara Cunha, Ines Reis, Susana Leitao, Cristina Costa, Soledade Ferreira, Teresa Teles  
Ginecologia E Obstetricia, Centro Hospitalar Entre O Douro E Vouga, Santa Maria Da Feira, Portugal

**Problem statement:** Malignant ovarian sex cord-stromal tumors (SCSTs) account for 8% of ovarian malignant neoplasms. Most patients are diagnosed with early-stage disease and prognosis is good. Granulosa cell tumors are the most common type of potentially malignant SCST. The objective of this paper is to describe two clinical cases with distinct clinical courses. **Results: Case 1:** 86 years old woman, found of two right pelvic masses with solid and

liquid areas detected on abdominopelvic Computed Tomography (CT) scan. Magnetic resonance imaging (MRI) detected a solid mass with cystic areas with 92x62x85mm, heterogeneous uptake of contrast, in the right adnexal region; without adenopathies or peritoneal implants. A complete surgery was performed, anatomopathological examination confirmed tumor of granulosa cells of the adult type, without capsule involvement. No metastasis on regional lymph nodes were detected. Favorable clinical course without recurrence at 6 months of follow-up. **Case 2:** 28 years old woman presented with abdominal pain and fever within five weeks of evolution. On gynecological examination, painful mobilization of the cervix and a mass occupying the pouch of Douglas. On transvaginal ultrasound (TVU), a nodular, bilobulated, heterogeneous formation with 106x99mm, without exuberant vascularization, was found. Analytically, increased inflammatory parameters. A diagnosis of pelvic inflammatory disease was assumed and treated. In the absence of clinical improvement with medical treatment, a laparoscopy was decided with finding of a pelvic mass suggestive of hemorrhagic cyst. A left annexectomy was performed and anatomopathological examination revealed tumor of granulosa cells of the adult type. However, two weeks later, patient was admitted due to uncontrolled pain. On TVU, free liquid lamina suggestive of implants and two masses in the adnexal regions. On staging CT scan, moderate volume ascites and findings suggestive of peritoneal carcinomatosis. Given clinical progression, MRI was performed which identified peritoneal carcinomatosis and hepatic metastasis. In oncologic group reunion, primary chemotherapy was decided. Despite therapy, progressive clinical deterioration with death within 6 months. **Conclusion:** SCSTs are rare tumors generally with favorable prognosis, but some are aggressive with lethal outcomes. These clinical cases represent two extremes of possible clinical courses in this type of tumors, reflecting the inherent clinical variability.

#### INTRAOPERATIVE USE OF INDOCYANINE GREEN TO DELINEATE PLACENTAL INVASION DURING ROBOTIC PERIPARTUM HYSTERECTOMY FOR MORBIDLY ADHERENT PLACENTA

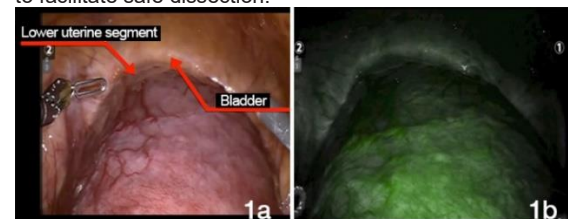
Katherine L. Dengler<sup>1</sup>, Payam Katebi Kashi<sup>2</sup>

<sup>1</sup>Division of Urogynecology, Department of Obstetrics and Gynecology, Walter Reed National Military Medical Center, Bethesda, USA

<sup>2</sup>Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Inova Fairfax Women's Hospital, Falls Church, USA

**Problem statement:** Morbidly adherent placenta (MAP) is one of the leading causes of postpartum hemorrhage. MAP involves the abnormal attachment of placental villi to the myometrium with the potential for deeper invasion of surrounding organs. The diagnosis is typically made by ultrasound and confirmed with magnetic resonance imaging, however there is limited intraoperative evaluation beyond gross visualization of the extent of invasion. Intravenous indocyanine green (ICG) has been used robotically to validate bowel integrity after anastomosis, confirm blood supply and could be utilized during surgical intervention of MAP, to highlight the magnitude of placental invasion. **Methods:** A 36 year-old gravida 4, para 2 evaluated at 17 weeks gestation with a history of a prior cesarean delivery, was diagnosed with morbidly adherent placenta. Ultrasound revealed an anterior placenta previa covering the entire cervix and extending over the posterior lower uterine segment with bleeding present in front of the placenta posteriorly. The patient was counseled regarding the risks and benefits of continued pregnancy versus a peripartum hysterectomy. The patient opted for surgical management, and given her stable presentation was offered a minimally invasive approach. **Results:** The DaVinci robot was docked, and the patient was given three milliliters of ICG followed by ten milliliters of sterile water

intravenously. The fluorescent system was activated to delineate the extent of placental blood flow from the lower uterine segment. The placenta had eroded through the uterus anteriorly, likely in the location of the patient's prior cesarean scar, but had not invaded the bladder (Figure 1 a, b). Bilateral ureterolysis was performed, and the uterine arteries were ligated. After finishing the hysterectomy, a D&E was performed in order to facilitate uterine removal vaginally. The vaginal cuff was closed robotically. The estimated blood loss was minimal, and patient was discharged home on postoperative day one without complication. **Conclusion:** Given advances in minimally invasive surgery, we propose a robotic-assisted approach instead of traditional open laparotomy as an effective technique for peripartum hysterectomy in selected patients. The addition of intravenous ICG can be utilized to assist visual identification of the extent of MAP during these cases to facilitate safe dissection.



1a: Morbidly Adherent Placenta (MAP) visible vessels through lower uterine segment

1b: Intravenous ICG showing the extent of MAP vascular involvement

#### OVARIAN CANCER: LIFESTYLE, DIET AND NUTRITION BY A. EL-SHERIF, S. EL-SHERIF, AH. TAYLOR, T. AYAKANNU NUTRITION AND CANCER, DOI:10.1080/01635581.2020.1792948

Sherif Elsherif<sup>2</sup>, Ahmed Elsherif<sup>1</sup>, Anthony Henry Taylor<sup>3</sup>, Ayakannu Thangesweran<sup>4</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Arrow Park Hospital, Upton, UK

<sup>2</sup>Department of Obstetrics and Gynaecology, West Cumberland Hospital, Whitehaven, UK

<sup>3</sup>Department of Molecular and Cellular Biology, University of Leicester, Leicester, UK

<sup>4</sup>Gynaecology Oncology Cancer Centre, Liverpool Womens NHS Foundation Trust, Liverpool, UK

**Background and aims:** Ovarian cancer is the leading cause of female reproductive cancer death. It is estimated that dietary habits accounts for 30% of all cancers with smoking (a lifestyle factor) being the leading preventable cause. This review sets out what we know about the food, nutrition and lifestyle factors that cause ovarian cancer, affect women with ovarian cancer and the problems associated with study design that may affect its prevention and patient survival. surgical and chemical interventions are also assessed. **Method:** Studies reporting lifestyle, diet, nutritional benefits in ovarian cancer patients from 1980 to date were examined. Insights into the potential problems related with study design evaluated. **Results:** Dietary content and the association between dietary patterns, body weight and energy imbalance are factors which may lie behind the mechanisms that have an impact on the risk of developing ovarian cancer. It has been suggested that high glycemic index and glycemic load can be associated with ovarian cancer development. Studies that have tried to assess the effect of circadian rhythm and plasma melatonin on the risk of ovarian cancer, have however been less than successful. Also, some surgical and chemical interventions, have been related to development of ovarian cancer. Although improvements in disease prevention and patient survival can be made through nutritional, dietary and lifestyle interventions, Uncertain evidence, resulting directly and indirectly from inadequate study design may negate

this. **Conclusions:** Lifestyle, dietary and nutrition interventions may prevent and improve survival of ovarian cancer patients. However, inadequate clarity and gaps exist within the literature e.g. study design, data interpretation, absence of cohesive questions and scoring systems. Future directions that emphasize high quality studies and clinical trials should be encouraged. **Disclosure statement:** The authors declare they have no known or perceived conflicts of interest related to this work.

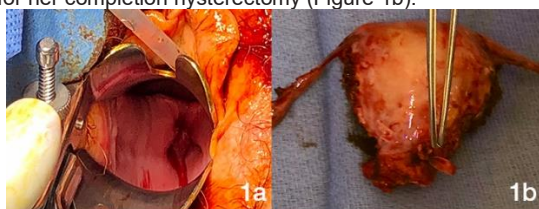
#### OVERCOMING CHALLENGES OF MINIMALLY INVASIVE EXTRAFASCIAL HYSTERECTOMY IN THE POST RADICAL TRACHELECTOMY PATIENT

Payam Katebi Kashi<sup>1</sup>, Katherine L. Dengler<sup>2</sup>

<sup>1</sup>Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Inova Fairfax Women's Hospital, Falls Church, USA

<sup>2</sup>Division of Urogynecology, Department of Obstetrics and Gynecology, Walter Reed National Military Medical Center, Bethesda, USA

**Problem Statement:** During radical trachelectomy extensive retroperitoneal dissection is performed for ureterolysis, parametrectomy and pelvic lymphadenectomy. The bladder is elevated away from the pubocervical fascia to take an adequate vaginal margin with the cervix which may result in scarring and significant anatomic changes. Extrafascial hysterectomy after radical trachelectomy can pose unique challenges including difficulty placing the uterine manipulator due to lack of cervical tissue or stenosis, dissecting the bladder due to dense adhesions, skeletonizing and transecting uterine arteries which may be in closer approximation to the ureters, and finally closing the vaginal cuff with proper apical support. **Methods:** A 40 year-old patient with prior stage IB1 cervical cancer who underwent fertility sparing robotic assisted radical trachelectomy, bilateral pelvic lymphadenectomy, and cerclage placement presented five years later for her completion hysterectomy after her childbearing was complete. She had annual surveillance with cervical pap tests which all had been negative for HPV, precancerous cells, and cervical cancer. She had regular menses since, without stenosis or hematometria (Figure 1a). The patient had been disease free for five years without signs of cancer recurrence, so a minimally invasive approach was chosen for her completion hysterectomy (Figure 1b).



1a: Post-trachelectomy utero-vaginal opening

1b: Hysterectomy specimen with cerclage knot

**Results:** Four steps were utilized to perform a robotic-assisted total hysterectomy, bilateral salpingectomy and cystoscopy. Step 1: The uterine manipulator was placed under direct visualization after laparoscopic port placement. Step 2: The bladder flap was created by utilizing a lateral to medial approach to carefully dissect the bladder off the lower uterine segment. Step 3: The uterine artery was skeletonized carefully to drop the ureter away, and the vessel was then transected using multiple bipolar and monopolar bites. Step 4: The vaginal cuff was closed while incorporating the uterosacral ligaments bilaterally to support the vaginal apex. **Conclusion:** The decision to perform hysterectomy in the post radical trachelectomy patient after completion of childbearing is a matter of debate

as long-term data is lacking comparing uterine preservation versus completion hysterectomy. If definitive surgery is desired, we demonstrate a reproducible four-step strategy to perform a safe and efficient hysterectomy in the post radical trachelectomy patient using a minimally invasive approach.

#### VULVAR CANCER AND SURGERY: PROGNOSTIC FACTORS AND OUTCOMES

Ionescu Sinziana<sup>1</sup>, Octavia Luciana Madge<sup>1</sup>, Dan Subtirelu<sup>1</sup>, Laurentiu Simion<sup>1</sup>, Claudiu Daha<sup>1</sup>, Marian Marincas<sup>1</sup>, Virgiliu Prunoiu<sup>1</sup>, Madalina Radu<sup>2</sup>, Radu Mitrica<sup>3</sup>, Eugen Bratucu<sup>1</sup>

<sup>1</sup>First Clinic of General Surgery and Surgical Oncology, Bucharest Oncology Institute, Bucharest, Romania

<sup>2</sup>Pathology Department, Bucharest Oncology Institute, Bucharest, Romania

<sup>3</sup>Radiotherapy Clinic, Bucharest Oncology Institute, Bucharest, Romania

**Problem statement** can be summarised by the fact that vulvar cancer is a rare gynaecologic neoplasm with important rates of patient morbidity and mortality.

**Methods:** We performed a retrospective study (from 01/01/2010 to 01/10/2020) in the First Clinic of General Surgery and Surgical Oncology of the Bucharest Oncology Institute, during which we identified 91 patients with vulvar cancer in different stages and further looked into the type of surgical procedures performed and the consecutive patient outcomes. One of the targets of the study was to identify a relationship between different prognostic factors such as: tumour stage, tumour grade, patient age, lymph node metastases on the one side, and on the other, disease free survival and overall survival rates. **Results:** From the total batch of 91 patients, radical vulvectomy (either unilateral or bilateral) was performed in 40 cases, in other 26 cases excisions were performed (of the vulvar lesions), and, in the rest of 25 cases, either partial excisions with the purpose of ensuring haemostasis were performed or radical radiotherapy was applied. Adjuvant radiotherapy was administered in 35 patients. The mean follow up time was 2 years (varying from 1 to 9 years), locoregional recurrence was 27% in the radical surgery group, 15% in the surgery plus radiotherapy group and around 50% in the radical radiotherapy group. Distant metastases rate was 8%.

**Conclusion:** Surgical interventions contributed to better local control rates in early stage vulvar cancer. Adjuvant radiotherapy was indicated in situations of nodal positivity or positive surgical margins. Radical radiotherapy can be taken into account and resorted to in patients with significant comorbidities.

#### THREE CANCERS (CERVIX, OVARY, RECTAL), ONE PATIENT: WHICH WILL RELAPSE? HOW MANY SURGERIES ARE TOO MANY?

Ionescu Sinziana<sup>1</sup>, Octavia Luciana Madge<sup>1</sup>, Dan Subtirelu<sup>1</sup>, Alexandru Grigorescu<sup>4</sup>, Radu Mitrica<sup>3</sup>, Madalina Radu<sup>2</sup>, Virgiliu Prunoiu<sup>1</sup>, Marian Marincas<sup>1</sup>, Claudiu Daha<sup>1</sup>, Eugen Bratucu<sup>1</sup>

<sup>1</sup>First Clinic of General Surgery and Surgical Oncology, Bucharest Oncology Institute, Bucharest, Romania

<sup>2</sup>Pathology Department, Bucharest Oncology Institute, Bucharest, Romania

<sup>3</sup>Radiotherapy Clinic, Bucharest Oncology Institute, Bucharest, Romania

<sup>4</sup>OnCology Department, Bucharest Oncology Institute, Bucharest, Romania

**Problem statement:** Could be obviated by the unusual case of three consecutive cancers (uterine cervix, ovary and rectal) and their series of relapses in one patient, in need for a series of surgical interventions, sometimes in emergency setting. **Methods:** We performed a detailed analysis of this case, which was operated on in the First

Clinic of General Surgery and Surgical Oncology of the Bucharest Oncology Institute, by looking into the details and by examining the clinical context in which a series of surgical interventions were required: in the beginning of the disease process for surgical oncologic reasons and further on, in the case of tumour relapse, in order to perform lifesaving interventions (as was the case for vaginal bleeding from a recurrence of the ovarian neoplasm, intestinal bowel obstruction and enterovaginal fistula). **Results:** The surgical personal patient history, in this case, is impressive: she was initially hysterectomised for a cervical tumour, a few years after she presented with an intraabdominal cystic tumour, which was diagnosed as ovarian cancer relapse, she underwent further chemotherapy and, afterwards, a rectal tumour was diagnosed and treated with preoperative radiotherapy and abdomino-perineal resection. This year she presented with a bleeding tumour at the level of the vagina which was biopsied and treated with radiofrequency ablation and afterwards a few months after the patient addressed the hospital in intestinal obstruction with an enterovaginal fistula. The fistular path was identified, it was in strict adherence to the pelvic floor, and the lesional process was shunted by an ileocaecal anastomosis. In the postoperative period, the patient developed an anastomotic leak and a median ileostomy was performed. **Conclusion** of this retrospective case analysis would lead towards the fact that, in such unusual cases, in which the surgeon must deal not with one major complication secondary to cancer relapse, but several and from different cancers, it becomes pertinent to try to solve the surgical emergency setting, even though it is no longer possible to cure the disease, in order to save the patient's life.

#### PERFORATION OF THE SIGMOID COLON – A RARE CLINICAL PRESENTATION OF THE OVARIAN TUMOR

Ana Soares, Vera Ribeiro, Henrique Morais, Nicole Cardoso, Antonio Lagoa, Antonio Lagoa  
Gynecologic Oncology Unit, University Hospital Center of Algarve, Faro, Portugal

**Problem statement:** 75% of the ovarian malignant tumors present themselves in advanced stages. The invasion of the colon's or rectum wall by the ovarian tumour isn't unusual, but its expansion to the intestinal mucous membrane is an extremely rare event. Hereby we'll describe a clinical case of a patient to whom have been diagnosed a perforation of the sigmoid colon due to an ovarian cancer. **Methods:** Clinical case review by calling up the computer file of the patient and scientific research. **Results:** We have described the clinical case of a woman, aged 81, who entered the E.R. reporting symptoms as abdominal pain, fever, diarrhea and vomiting, throughout the last month. During the objective examination of the patient a large pelvic tumor was found and the blood test results shown that the inflammatory parameters were high. An abdominal-pelvic CT was made and it revealed an heterogenous mass containing liquid and gas, measuring 120x80mm without cleavage from the sigmoid colon. The colonoscopy confirmed the presence of an ulcerated lesion with 6cm which has biopsied itself, meaning infiltration by undistinguished carcinoma. After the patient was stabilized, she had an exploratory laparotomy in order to get a citoreduction surgery, with the complete excision of the lesion. The patient also had a total hysterectomy with double anexectomy and a rectum-sigmoid resection (Hartmann surgery). A complete citoreduction was achieved. None postoperative complications were reported. The anatomopathological study revealed a serous ovarian tumour; stage IIB. Considering the patient's comorbidities, the multidisciplinary team decided to keep the patient under an active surveillance, in spite of giving her chemotherapy. **Conclusion:**

The rectum-sigmoidal perforation with signs of abdominal inflammation and sepsis can be evidence of ovarian cancer, demanding high suspicion abilities to achieve the right diagnosis. This case reinforces the importance of having a multidisciplinary team working on the diagnosis, treatment and guidance of the patients with ovarian cancer at an Oncogynaecological service.

#### POSTMENOPAUSAL INVASIVE MOLE WITH UTERINE RUPTURE

Marina Sousa Gomes<sup>1</sup>, Mariana Vide Tavares<sup>2</sup>, Vanda Patricio<sup>2</sup>, Daniel Fernandes<sup>2</sup>, Almerinda Petiz<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Alto Minho Local Healthcare Unit, Viana do Castelo, Portugal

<sup>2</sup>Department of Obstetrics and Gynaecology, Portuguese Institute of Oncology - Porto, Porto, Portugal

**Problem statement:** Postmenopausal gestational trophoblastic neoplasia (GTN) is extremely rare and its definite pathogenesis is controversial. **Methods:** The authors describe a case of postmenopausal invasive mole presenting with uterine rupture. **Results:** Fifty-one-year-old female, gravida 1, para 1, postmenopausal for 4 years, present with a history of vaginal bleeding of three months duration. Ultrasound uterine evaluation showed a heterogeneous mass with anechoic spaces with 15.1 x 12.4 x 10.0 cm. A complete mole was diagnosed on endometrial biopsy. She was referred to the gynecological oncology center. The patient had a healthy previous medical history. She was sexually active. Surgical treatment was proposed. Before surgery, she developed abdominopelvic pain. Clinical examination showed pain in the hypogastric area with a rebound. According to the hematological laboratory examination, Hb was 5.3 g/dl. Her pre-evacuation serum b-hCG was 365806 mIU/ml. Two red blood cell units were administered before surgery. The patient underwent exploratory laparotomy showing an extensive hemoperitoneum caused by a complete uterine rupture on the right side and the left isthmus area, figure 1. Extensive right parametrial involvement was noted. Due to profuse hemorrhage, she underwent total hysterectomy with bilateral salpingo-oophorectomy, and right hypogastric ligation was performed, figure 2. Four red blood cell units and one fresh frozen plasma unit were administered during surgery. Two weeks after surgery serum b-hCG was 613 mIU/ml. Histopathology confirmed the diagnosis of an invasive mole. Complete uterine rupture in the isthmus area and right uterine side were identified. Right parametrial involvement was confirmed. Lymphovascular invasion was noted. In postoperative imagiologic studies, no metastatic lesions were found. Serum b-hCG on postoperative day 28 was 475 mIU/ml. This patient was treated with methotrexate. **Conclusion:** To our knowledge, our case is the first description in the world literature of an invasive mole in a postmenopausal woman complicated with uterine rupture. In postmenopausal women, the exact diagnosis of GTN can be difficult, because of its rarity and presentation in unusual situations. Early diagnosis of uterine perforation in this case and adequate management were crucial for a better prognosis.

#### GYNECOLOGY

##### ENDOMETRIAL RECEPTIVITY CHARACTERISTICS IN WOMEN WITH DIFFERENT FUNCTIONAL ACTIVITY OF OVARIAN CORPUS LUTEUM

Natalia Aganezova<sup>1</sup>, Sergey Aganezov<sup>1</sup>, Anastasia Kuzmina<sup>1</sup>, Ksenia Gogichashvili<sup>1</sup>, Alexander Baldin<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, I.I. Mechnikov North-Western State Medical University, St-Petersburg, Russia

<sup>2</sup>Chief physician, Center for family planning and reproduction, St-Petersburg, Russia

**Objective:** To study the endometrial expression of estrogen (ER) and progesterone (PR) receptors in women with different functional activity of ovarian corpus luteum (OCL) (serum progesterone (P) level (nmol/l): 16.1±P. **Materials and methods:** There were main (I) (121 patients with infertility (n=81) and miscarriages (n=40) in the anamnesis) and control (II) groups (16 healthy women) (20-40 y.o.). We performed endometrial biopsy and obtained peripheral blood (6-8th day after ovulation), conducted histological and immunohistochemical (ER, PR expression) analysis of endometrium samples. **Results:** All women had ovulatory menstrual cycle ( $P \geq 16.1$  nmol/l); serum estradiol (E2) level (pmol/l) was 692.2±29.1 (I) vs 707.4±66.1 (II); P (nmol/l) – 45.1±2.0 (I) vs 39.1±4.9 (II) ( $p_{0.05}$  for all cases). Mid-secretory endometrium was determined in healthy women and in 42% (n=51) in the main group. All healthy women and 44% (n=53) in II group showed low glandular ER, PR expression, reduced stromal ER expression, high PR stromal expression in endometrium. In 69 women with normal hormone-receptor endometrial interactions (n=16 in I, n=53 in II) serum  $P_{0.05}$  for all cases). In 56% (n=68) of women in the main group with disturbed endometrial 'response' low activity of OCL was observed in 25% (n=17), high – in 75% (n=51) of cases. No significant differences were found in ER, PR H-score count in dependence of high (1) or low (2) activity of OCL: ER in glands 204.2±10.7 (1) vs 236.1±16.7 (2), ER in stroma 174.0±11.7 (1) vs 157.2±21.8 (2), PR in glands 239.0±9.2 (1) and 231.7±22.7 (2), PR in stroma 271.6±3.8 (1) vs 271.1±7.5 (2) ( $p_{0.05}$  for all cases). **Conclusions:** Higher serum P level was not determined as a factor correlating with higher frequency of normal hormone-receptor endometrial interactions.

#### RETAINED PRODUCTS OF CONCEPTION FOLLOWING SURGICAL MANAGEMENT OF CERVICAL ECTOPIC PREGNANCY

Marrwah Ahmadzai, Rebecca Yuan Li, Danica Vress, Sumi Saha  
Obstetrics and Gynaecology, The Canberra Hospital, Canberra, Australia

**Background:** Cervical pregnancy, wherein the pregnancy implants in the endocervical canal, accounts for fewer than 1% of ectopic pregnancies (1). Cervical pregnancy may cause catastrophic haemorrhage that can necessitate hysterectomy and hence cause infertility (1). Risk factors include in-vitro fertilisation, previous dilatation and curettage, Asherman's syndrome and indwelling intrauterine devices (2). Due to its rarity, evidence regarding management is limited. **Case:** A 36-year-old otherwise well primiparous female presented with spontaneously conceived pregnancy. She had never used hormonal contraception and had no previous gynaecological history. Following a dating scan at seven weeks, she was referred to the local hospital for suspected threatened miscarriage, as the gestational sac was seen within the endocervical canal. Her symptoms were occasional light vaginal spotting. An interval scan attended nine days later revealed a live pregnancy with a crown-rump length of 17.5mm and a fetal heartbeat with the gestational sac within the cervix. Her  $\beta$ -hCG was 118,065IU/L. She underwent ultrasound guided dilatation and suction curettage. Due to brisk bleeding, an intrauterine balloon was inserted and Tranexamic acid and uterotonics were given. She had an estimated blood loss of 1000mL. Her post-operative course was complicated by asymptomatic hypotension for which she was admitted to the intensive-care unit and was treated with blood transfusion. At six-weeks follow-up, she reported ongoing bleeding and repeat ultrasound revealed retained products of conception measuring 47x22mm on transvaginal ultrasound. Following unsuccessful medical management with Misoprostol, she had a repeat dilatation and curettage fifty-one days after her initial surgery. She lost a further 400mL of blood and had an intrauterine balloon inserted.

**Discussion:** This is an unusual case of ectopic pregnancy in a woman with no risk factors. The case highlights the challenges in differentiating between a cervical pregnancy and miscarriage. Repeat short term ultrasound in 2-3 days and serum  $\beta$ -hCG monitoring has demonstrated utility in diagnosis (3). Although optimum management of cervical pregnancy is unknown, early diagnosis allows consideration of conservative management approaches, which may be safer in earlier gestations, as the risk of heavy bleeding necessitating hysterectomy in a dilatation and curettage is up to 40% (4).

#### A RARE CASE OF LABIAL CAVERNOUS LYMPHANGIOMA

Marrwah Ahmadzai, Rebecca Yuan Li, Peter Scott  
Obstetrics and Gynaecology, The Canberra Hospital, Canberra, Australia

**Background:** Lymphangiomas are benign tumours of the lymphatic vessels that are usually found in the head and neck (1). Vulvar lymphangiomas are rare and may be classified based on location of lymphatics as either lymphangioma circumscriptum which is superficial or cavernous (also known as cystic) lymphangioma which is deep (2). Only ten cases of cavernous lymphangioma have been reported globally (3). Lymphangiomas may be congenital or acquired secondary to radiation, trauma, or tuberculosis (2). Complete surgical resection is the treatment of choice (4). **Case:** A 23-year-old otherwise well nulliparous female presented to the emergency department with a ten-week history of left labial pain. She had initially noticed a painless swelling in her left labia. She then developed intermittent pain and her symptoms gradually worsened. She now had constant pain. She had been managed conservatively with antibiotics prior to presentation. The lesion was not discharging, and she was systemically well. She had no history of trauma or surgery to the site. She had never had a cervical screening test and was not sexually active. On examination, she was hemodynamically stable and afebrile. There was a 3cm clear cyst on her left labia majora that was soft and fluctuant. She had a normal leucocyte count and differential and inflammatory markers. Under general anaesthesia, the cyst was marsupialised. Two weeks later, she presented with recurrence of symptoms. The swelling on her labia had increased in size and she had worsening pain. She remained systemically well. Her wound was healing well and was not discharging. She was commenced on oral antibiotics and managed conservatively. As her symptoms did not improve, however, she eventually underwent repeat marsupialisation two months following her initial surgery. Histopathology was consistent with cavernous lymphangioma. **Discussion:** This case contributes to the small body of literature about vulvar cavernous lymphangioma and reflects features described in previous case reports. That is, cavernous lymphangiomas occur in reproductive aged women and almost always occur in the labia majora (3). These tumours are difficult to completely excise as they often have unclear margins hence recurrence is likely, as seen in this case (5).

#### NEXT GENERATION VACUUM-BASED CERVICAL TENACULUM, AN ATRAUMATIC DEVICE THAT REDUCES THE PAIN AND BLEEDING ASSOCIATED WITH FREQUENT GYNAECOLOGICAL PROCEDURES

Andrea Albornoz<sup>2</sup>, Julien Finci<sup>1</sup>

<sup>1</sup>Chief Technology Officer, ASPIVIX, Lausanne, Switzerland

<sup>2</sup>Business Development, Aspivix, Lausanne, Switzerland

Unintended pregnancies are a global epidemic. 1. They are associated with substantial costs to healthcare systems, social services as well as significant emotional distress to women, and their families. 2. Worldwide, about 85 million

pregnancies, representing 44 % of all annual pregnancies are unintended. 3,4. Of these pregnancies 50 % end in abortion, 12 % end in miscarriage, and 38 % result in unplanned births. 5. In the US alone, the annual excess costs to the economy is about 11 billion US dollars. 6. Up to 100,000 maternal deaths could be avoided each year if women who did not want children used effective contraception. 3 40% of the unintended pregnancies are a result of contraceptive failure or incorrect use. 3 If contraception need was fully satisfied, 53 million unplanned pregnancies could be prevented. 3 The Intrauterine Device (IUD) is considered the most cost-effective reversible contraceptive solution. 7,8,9. Fear of severe pain during IUD placement remains a significant adoption barrier for women. 10,11,12. Several attempts to reduce pain and bleeding have been reported in the literature such as changing the design of tenaculum. 13, applying anaesthetics, without much success. 10,14 .A next-generation, patent protected vacuum-based cervical device that delivers the same manoeuvrability as the tenaculum without the reported patient trauma related to pain, bleeding and tissue tear would support IUD adoption. 15. Results from "First in Women" Trial in Switzerland are expected in 2H2020.

#### RELUGOLIX COMBINATION THERAPY SIGNIFICANTLY REDUCED MENSTRUAL BLOOD LOSS WITH FIRST TREATMENT CYCLE IN WOMEN WITH HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS: LIBERTY PHASE 3 PROGRAM RESULTS

Roberta Venturella<sup>1</sup>, Ayman Al-Hendy<sup>2</sup>, Andrea S. Lukes<sup>3</sup>, Yulan Li<sup>4</sup>, Laura McKain<sup>4</sup>, Elizabeth A. Stewart<sup>5</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Magna Graecia University of Catanzaro, Catanzaro, Italy

<sup>2</sup>Department of Obstetrics and Gynecology, University of Illinois/Chicago, Chicago, USA

<sup>3</sup>Obstetrics and Gynecology, Carolina Woman's Wellness Center, Durham, USA

<sup>4</sup>Clinical Development, Myovant Sciences Inc., Brisbane, USA

<sup>5</sup>Obstetrics & Gynecology, Mayo Clinic, Rochester, USA

**Problem statement:** Heavy menstrual bleeding (HMB) is the most clinically significant symptom of uterine fibroids (UF) and can have a negative impact on women's lives.

**Methods:** LIBERTY 1 and 2 were multinational, randomized, double-blind, placebo-controlled studies that evaluated the effect of Relugolix Combination Therapy (Rel-CT: relugolix 40 mg [an oral gonadotropin-releasing hormone receptor antagonist], estradiol 1 mg, norethindrone acetate 0.5 mg) on UF-associated HMB. The primary endpoint was a menstrual blood loss (MBL) volume 80 mL and a ≥50% reduction in MBL volume from baseline. Reduction in MBL volume was a predefined secondary endpoint. Premenopausal women (age 18–50 years) with ultrasound-confirmed UF and MBL ≥80 mL per cycle (assessed by the alkaline hematin method) were randomized to Rel-CT (n=254), Delayed Rel-CT (relugolix 40 mg monotherapy for 12 weeks then Rel-CT for 12 weeks, n=259), or placebo (n=257) for 24 weeks. Time to treatment response was assessed by MBL volume using collections of feminine products and subsequent alkaline hematin extraction. Pooled results from the LIBERTY 1 and 2 modified intention-to-treat populations for Rel-CT (n=253) and placebo (n=256) are presented. **Results:** Women in LIBERTY had a mean (standard deviation) baseline MBL volume of 228.8 (154.3) mL. In the Rel-CT group, a significantly greater mean percent reduction of 52.4% in MBL volume was observed in the first menstrual cycle vs 14.7% for placebo (p<0.0001). By the second menstrual cycle, MBL volume reduction was 80.2% with Rel-CT vs 11.6% for placebo (p<0.0001). The improvement was sustained through to end of treatment (EOT; 24 weeks), when the observed mean reduction in MBL volume in the Rel-CT group was 84.7% (65.2% higher than placebo;

p<0.0001). Of women treated with Rel-CT, 72.3% met the primary endpoint. The differences in the proportion of patients meeting the primary endpoint were statistically significant and clinically meaningful between Rel-CT and placebo groups from the Week 4 visit through to EOT (p<0.0001). **Conclusion:** A rapid clinically meaningful response – demonstrated by significant reduction in MBL volume – was observed in patients treated with once-daily Rel-CT vs placebo after 1 month and maintained throughout the treatment period. Study funded by Myovant Sciences, Inc.

#### LIBERTY: LONG-TERM EXTENSION STUDY DEMONSTRATING ONE-YEAR EFFICACY AND SAFETY OF RELUGOLIX COMBINATION THERAPY IN WOMEN WITH SYMPTOMATIC UTERINE FIBROIDS

Ayman Al-Hendy<sup>1</sup>, Andrea S. Lukes<sup>2</sup>, Alfred Poindexter III<sup>3</sup>, Roberta Venturella<sup>4</sup>, Claudio Villarroel<sup>5</sup>, Rachel B. Wagman<sup>6</sup>, Yulan Li<sup>6</sup>, Laura McKain<sup>6</sup>, Elizabeth A. Stewart<sup>7</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, University of Illinois/Chicago, Chicago, USA

<sup>2</sup>Obstetrics and Gynecology, Carolina Woman's Wellness Center, Durham, USA

<sup>3</sup>Department of Obstetrics and Gynecology, Baylor College of Medicine and St. Lukes Episcopal Hospital, Houston, USA

<sup>4</sup>Department of Obstetrics and Gynecology, Magna Graecia University of Catanzaro, Catanzaro, Italy

<sup>5</sup>Instituto de Investigaciones Materno Infantil (IDIMI), University of Chile, Santiago, Chile

<sup>6</sup>Clinical Development, Myovant Sciences Inc., Brisbane, USA

<sup>7</sup>Obstetrics and Gynecology, Mayo Clinic, Rochester, USA

**Problem statement:** Uterine fibroids (UF) are common and can have a substantial negative impact on women's lives; however, there is currently a lack of long-term medical treatment options. **Methods:** The long-term extension study was a 28-week, multinational, Phase 3, open-label trial in which women with UF-associated heavy menstrual bleeding (HMB) who completed the 24-week, double-blind, placebo-controlled LIBERTY 1 and 2 trials were eligible to enroll. All received once-daily Relugolix Combination Therapy (Rel-CT: 40 mg relugolix [an oral gonadotropin-releasing hormone receptor antagonist], estradiol 1 mg, norethindrone acetate 0.5 mg). The primary efficacy endpoint was the proportion of women achieving or maintaining a menstrual blood loss (MBL) volume 80 mL and a ≥50% reduction from parent study baseline to the last 35 days of treatment, measured by the alkaline hematin method. Secondary endpoints included mean percentage MBL reduction, amenorrhea rate, and improvements in anemia. Adverse events (AEs) and bone mineral density (BMD) changes by dual-energy X-ray absorptiometry were assessed. The Rel-CT group had the longest treatment duration (52 weeks); the other groups, where patients transitioned to Rel-CT, are supportive. **Results:** Of the 770 randomized LIBERTY patients, 610 completed the primary study; 477 (78%) enrolled in the extension and 363 (76%) completed. The Rel-CT group demonstrated sustained improvement in HMB through 52 weeks, with 87.7% of patients meeting the definition of responder. Mean MBL volume reduction from baseline was 89.9%, with most patients (70.6%) achieving amenorrhea. MBL reductions led to substantial improvements (2 g/dL) in hemoglobin concentrations at Week 52 for most (59.0%) patients with anemia (10.5 g/dL) at baseline. Reductions in uterine and UF volume at Week 24 were sustained through Week 52. AE incidence in the Rel-CT group was consistent through the 52-week period. There were no clinically meaningful changes in BMD, and a mean percentage reduction of –0.80% (95% confidence interval: –1.36, –0.25) for lumbar spine at Week 52. **Conclusion:** Rel-CT showed durability of effect for HMB through 52 weeks of treatment in women with UF. No new safety signals were identified, and bone mass was maintained. Study funded by Myovant Sciences, Inc.

## ACUPUNCTURE AND FEMALE ESTROGEN LEVELS: A LITERATURE REVIEW OVER STUDIES PUBLISHED IN THE LAST 5 YEARS

Diogo Calado<sup>1</sup>, Joao Cruz<sup>1</sup>, Domingos Branco Vaz<sup>3</sup>, Tatiana Branco Vaz<sup>2</sup>

<sup>1</sup>Biomedical Sciences, School of Health of Polytechnic institute of Setubal, Setubal, Portugal

<sup>2</sup>Gynecology / Obstetrics, Amamentos Clinic, Lisbon, Portugal

<sup>3</sup>Gynecology / Obstetrics, Hospital da Luz, Lisbon, Portugal

**Problem statement:** The contact of the western world, and Europe in particular, with acupuncture is not recent, with a greater focus on the study of the mechanisms of action in the intervention and management of pain. In recent years, several researchers have sought to analyze the influence of acupuncture on the levels of female endogenous estrogens. If evidence is found on the action of acupuncture at this level, being a safe intervention with few side effects, it may be considered as a complementary therapy in the treatment of clinical conditions that present low levels of endogenous estrogens. The objective is to analyze the literature published on Pubmed which establishes a link between acupuncture and the levels of female estrogens.

**Methods:** The database used was Pubmed-Mesh, and the search was performed using the following keywords with the following search strategy: "Acupuncture" [Mesh] OR "Acupuncture Therapy" [Mesh] OR "Acupuncture Points" [Mesh] AND "Estrogens" [Mesh] in August 2020. **Results:** A total of 38 articles were found and the literature was analyzed and merged. **Conclusion:** After analyzing the articles found, a consistent increase in serum estradiol levels was observed with acupuncture and electroacupuncture intervention in specific acupuncture points. It should, however, be noted that all these studies were performed on animal models. It seems pertinent to perform this line of research in humans, which may allow a better understanding of this relationship and its mechanisms, as well as to design intervention strategies in specific situations in which the elevation of serum estradiol levels may have a therapeutic effect.

## ACUPUNCTURE AND PROLACTIN LEVELS: A LITERATURE REVIEW PUBLISHED IN THE LAST 10 YEARS

Tatiana Branco Vaz<sup>2</sup>, Domingos Branco Vaz<sup>3</sup>, Joao Cruz<sup>1</sup>, Diogo Calado<sup>1</sup>

<sup>1</sup>Biomedical Sciences, School of Health of Polytechnic institute of Setubal, Setubal, Portugal

<sup>2</sup>Gynecology / Obstetrics, Amamentos Clinic, Lisbon, Portugal

<sup>3</sup>Gynecology / Obstetrics, Hospital da Luz, Lisbon, Portugal

**Problem statement:** The World Health Organization recognizes breastmilk as the ideal food for babies, also benefiting their mothers. It also states that it is an effective way to ensure child health and survival and should be given in exclusive for the first six months of life. Several researchers have sought to analyze the influence of acupuncture on the levels of prolactin. If evidence is found on the action of acupuncture at this level, it may be considered as a complementary therapy in the promotion of breastfeeding. The objective is to analyze published literature on Pubmed which establishes a link between acupuncture and the levels of prolactin. **Methods:** The database used was Pubmed-Mesh, and the search was performed using the following keywords with the following search strategy: "Acupuncture" [Mesh] OR "Acupuncture Therapy" [Mesh] OR "Acupuncture Points" [Mesh] AND "Prolactin" [Mesh] in August 2020. **Results:** A total of 7 articles were found and the literature was analyzed and merged. **Conclusions:** After analyzing the articles found, a consistent increase in serum prolactin levels was observed with acupuncture intervention in specific acupuncture

points. It seems pertinent to continue clinical investigation, which may allow a better understanding and validation of its mechanisms, as well as to design intervention strategies to promote elevation of prolactin levels and consequently milk production.

## CERVIX LENGTH IN NON-PREGNANT WOMEN

Carolina Carneiro, Sara Cunha, Ines Reis, Catia Rodrigues, Susana Leitao, Teresa Teles  
Servico Ginecologia E Obstetricia, Centro Hospitalar Entre O Douro E Vouga, Santa Maria Da Feira, Portugal

**Problem statement:** Cervix length (CL) is part of the routine of gynecologic ultrasound and it's important in special pregnant populations to evaluate the risk of preterm birth. There're multiple studies describing normal curves for short cervix on pregnant woman; cut-off usually used to describe a short cervix is 25 mm in second trimester ultrasound. Regarding non-pregnant women, the values considered normal are not so clearly studied, which prevents the full appreciation of an ultrasound finding of a cervix considered short in an asymptomatic pregnant woman. However, the majority of publications refer to values of 25 mm or half of the size of the uterus body in premenopausal women. The objective of our work was to find a normal interval for CL in our population. **Methods:** Retrospective analysis of clinical processes with gynecology ultrasound in our institution during the period from January 2019 to July 2020. We analyze demographic characteristics from our population. **Results:** We obtained 1268 gynecology ultrasounds, excluding 59 repeated clinical processes. Our population of study included 1209 women with a median of age of 50 (SD  $\pm$  13,4) years. Regarding uterine measurements, the mean for cervix length was 30,7mm (SD  $\pm$  6,6mm), with values of 19,9mm and 39,0mm for 5th and 90th percentiles, respectively. Dividing the sample into two groups with the 50-year-old cut-off, we noticed that there were statistically significant differences in measurements of CL, as well as the other measurements of the uterus, with lower values in the group of older women (32 vs. 28 mm, p0,05). **Conclusion:** CL has an important role in evaluating risk of preterm labour in pregnant women. Although the cut-off usually used to describe a short cervix in pregnancy is 25 mm, normal CL in non-pregnant woman isn't totally defined. Our results have a subtle difference from that described in the literature, with a mean of 30,7 mm for CL, in accordance with cut-offs used in pregnancy.

## IS MONOTHERAPY OVARIAN STIMULATION BETTER THAN ADMINISTERING A COMBINATION OF TWO GONADOTROPINS?

Maria Cruz, Vanessa Vergara, Maria Eugenia Ruiz, Irene Rubio, Antonio Requena  
Medical Affairs, IVI Madrid, Madrid, Spain

	HP-hMG (n=1744)	rFSH (n=3384)	HP-hMG + rFSH (n=3840)	P
Age (y)	34.1 $\pm$ 0.2	31.1 $\pm$ 0.1	34.1 $\pm$ 0.1	<0.0001*
AMH (ng/ml)	2.9 $\pm$ 0.5	3.7 $\pm$ 0.4	2.8 $\pm$ 0.4	<0.0001*
MC	12.7 $\pm$ 1.5	14.1 $\pm$ 2.0	11.8 $\pm$ 1.6	<0.0001*
Stimulation (d)	11.1 $\pm$ 1.0	7.1 $\pm$ 0.7	8.8 $\pm$ 0.5	0.0001*
Cholesterol (mg/dl)	221.1 $\pm$ 100	203.1 $\pm$ 100	203.1 $\pm$ 100	0.538
OHSS (%)	1.536 $\pm$ 10	1.799 $\pm$ 40	1.935 $\pm$ 10	<0.0001*
OHSS (d)	10.0 $\pm$ 0.3	10.4 $\pm$ 0.3	10.4 $\pm$ 0.3	<0.0001*
OHSS	2.1 $\pm$ 0.2	2.2 $\pm$ 0.5	2.1 $\pm$ 0.2	<0.0001*
Subclinical OHSS	15%	10%	10%	0.079 *
Subclinical OHSS	30%	30%	30%	0.001*
Subclinical OHSS	20%	20%	40%	0.004 *
Implantation rate	44.5%	41.7%	42.7%	0.004*
Pregnancy rate	57.1%	54.3%	55.5%	0.002 *
Miscarriage rate	5.9%	6.0%	7.0%	0.314
OR	0.89	0.23%	0.23%	0.002*

\* Significantly different from HP-hMG/MH-rFSH protocol

\* Significantly different from Mix of rFSH+HP-hMG protocol

\* Significantly different from HP-hMG + rFSH protocol

**Problem statement:** To evaluate if the administration of a gonadotropin combination is more effective than a monotherapy in a population of young women. **Methods:** Retrospective anonymized cohort analysis performed in 11 Spanish-clinics from the IVI group. Women 38 years-old receiving monotherapy with HP-hMG (n=1744) or rFSH  $\alpha/\beta$  (n=3316) vs a mix of rFSH+HP-hMG (n=3840), with a FSH:LH activity ratio 1:1, 1:0 and 2:1, respectively. Patients underwent short antGnRH protocol, 0.25mg daily doses

from day 6 of stimulation. On day cycle 2/3, they received rFSH or HP-hMG or a mix of FSH+HP-hMG daily. Initial doses were based on weight and BMI according to the experience of clinicians. A single dose of 0.1mg GnRH agonist was used for triggering. Embryo transfer was performed on day 3/5. ANOVA and Chi-squared statistical analysis was performed. **Results:** Women in the mix protocol had significantly lower ovarian reserve than rFSH group. The effectiveness of the cycle in terms of retrieved, mature oocytes and according usable blastocyst rate was significantly lower for mix protocol vs the others (38% HP-hMG vs 36% rFSH vs 34% HP-hMG+rFSH). The clinical results as the implantation (44.9% HP-hMG vs 41.7% rFSH vs 42.2% Mix,  $p=0.044$ ), clinical pregnancy (57.1% HP-hMG vs 54.1% rFSH vs 55.5% Mix,  $p=0.035$ ) and live birth (45.8% HP-hMG vs 42.1% rFSH vs 43.5% Mix,  $p=0.023$ ) rates did not increase significantly with respect to the other two study groups. **Conclusions:** Assuming the limitation of the study design, the data derived from this retrospective study suggests that rFSH+HP-hMG co-administration with FSH:LH activity ratio 2:1, is a less viable option than the independent administration of these gonadotropins for young women. The mix of two gonadotropins implies a greater amount of medication, a fact that may have an impact on the cost of the treatment, making this protocol a less economically attractive strategy. We could assume that combining the strength of rFSH -in recruitment/follicular growth- together with the benefits-in oocyte maturation-derived from LH/hCG activity does not significantly improve the yielding of the treatment when a ratio 2:1 of FSH:LH activity is used, as it does when the ratio is 1:1.

#### SAFETY AND EFFICACY OF A PRODUCT CONTAINING PEA PROTEIN, GRAPE SEED EXTRACT AND LACTIC ACID ADMINISTERED AS AN ADD-ON THERAPY TO CLOTRIMAZOLE IN SUBJECTS WITH VULVOVAGINAL CANDIDIASIS: A MULTICENTRE, RANDOMIZED, CROSSOVER, DOUBLE-BLIND STUDY

Cristian Gainaru

General Medicine, Individual Medical Office, Corbii Mari, Romania

**Problem statement:** Vulvovaginal candidiasis (VVC) is frequently encountered in clinical practice with 75% of women having at least one episode during their lifetime. Among these, 5-10% experience more than three episodes per year, which is defined as recurrent vulvovaginal candidiasis (RVVC). Antifungals are recommended for the management of both VVC and RVVC with prolonged treatments particularly common for RVVC. With increasing drug resistance, alternative therapies with a different mechanism of action are needed to effectively increase antifungal action and prevent recurrences. This study evaluates the therapeutic effect of a non-pharmacological product containing substances of natural origin – pea protein, grape seed extract and lactic acid (PP+GSE+LA) – in association with clotrimazole in women diagnosed with vaginal yeast infection. **Methods:** A randomized, double-blind, multicentre study was performed with 48 female subjects diagnosed with VVC randomly assigned (1:1). A product containing PP+GSE+LA or LA alone were administered intravaginally for 7 days as adjuvant treatment concomitantly with clotrimazole vaginal tablets during the first 3 days. Efficacy was evaluated by measuring mycological count and vaginal pH. Safety was assessed by monitoring the occurrence of undesirable systemic or local effects reported by the patients. **Results:** PP+GSE+LA significantly increased antifungal efficacy by reducing mycological count by 88% from day 1 to day 7 ( $p=0.001$ ). PP+GSE+LA was significantly more effective than LA by 73% in mycological count reduction at day 7 ( $p=0.002$ ) and only the PP+GSE+LA arm is proven to restore the physiological pH of the vagina at the end of study. No side effects were reported during the entire study period. **Conclusion:** PP+GSE+LA proved to be a safe and

effective adjuvant treatment for vaginal yeast infection. Particularly, the product containing PP+GSE+LA was proven to effectively eradicate *C. albicans* and restore the physiological vaginal pH for the management of VVC and prevention of recurrences.



Young Scientist Abstract

#### TOTAL LAPAROSCOPIC HYSTERECTOMY WITHOUT UTERINE MANIPULATOR “KAMRAN'S TLH” : A SURGICAL VIDEO AND A RETROSPECTIVE ANALYSIS OF 86 PATIENTS

Ahmed Gendia, Waseem Kamran

Gynecology Surgery, Beacon Hospital, Dublin, Ireland

**Problem statement:** Total Laparoscopic hysterectomy (TLH) remains a common approach among laparoscopic surgeons. however, it depends on the use of uterine manipulator to facilitate the surgery. Although many studies reported the effectiveness of TLH with uterine manipulator, only few reported TLH without the use of any uterine or vaginal manipulation. Through A surgical video, we will demonstrate a safe and easy to learn technique to perform total laparoscopic hysterectomy without the use of uterine or vaginal manipulation. Additionally, the outcomes of 86 consecutive hysterectomies utilizing our approach. **Methods:** surgical technique will be demonstrated through a short video highlighting the easy to learn and safe to apply surgical steps. Additionally, the data of 86 patients who underwent KTLH for benign condition was retrospectively analysed. the data included intra- and postoperative finding , recovery and complications. **Results:** A total of 86 hysterectomies were performed utilizing the Kamran's TLH ( KTLH). Mean age was 52.2 ( $\pm 11$ ) years old and BMI was 28.2( $\pm 7$ ). Mean operative time was 64.7( $\pm 27.9$ ) minutes and estimated bloods loss was 46.2( $\pm 54.6$ ) ml. No intraoperative complications were recorded and there was no conversion to open surgery. Only one patient required readmission and surgery for vaginal vault dehiscence. **Conclusion:** Our experience in total laparoscopic hysterectomy demonstrated a safe, feasible and easily reproducible technique without the use of any uterine or vaginal manipulation that can be adopted universally by trainee and already practicing surgeon as well.

#### THE CLINICAL FEATURES OF WOMEN WITH GENITAL ENDOMETRIOSIS

Aynura Ismayilova, Jamila Qurbanova, Aytan Badalova

Gynecology, Scientific Research Institute of Obstetrics and Gynecology, Baku, Azerbaijan

Genital endometriosis is the leading medical and social problem of modern gynecology and indicates the feasibility of conducting a comprehensive clinical study of women of reproductive age with this pathology using modern diagnostic methods, which served as the purpose of conducting research work. The study involved 120 women of reproductive age with genital endometriosis. The examined patients were divided into the groups: Group I (retrospective studies) consisted of  $n = 70$  patients with genital endometriosis; Group II (prospective studies) consisted of  $n = 50$  patients with this disease; Control group III (CG) consisted of  $n = 30$  conditionally healthy fertile women without this pathology. The average age of women was  $35 \pm 15$  years. The following methods were carried out: clinical, laboratory; instrumental and special research methods, an assessment of the state of health by functional systems. Scales were used: visual analogue scale (VAS) according to the IMMPACT recommendation (1998) to assess pain symptoms. The intensity of pain syndrome was assessed by us using a visual analogue scale (VAS, 1998), which allowed us to quantify pain symptoms in this contingent of patients: mild (1-3 points) of pain experienced

was observed in 54 (45%) patients, moderate (4-7 points) - in 56 (46.7%), severe (unbearable pain - 8-10 points) - in 10 (8.3%) patients. Intolerable pain was observed in patients requiring mandatory administration of analgesics in 10 (8.3%), which were more often observed in patients of both groups: 7 (10%) in group I, while in group II it was noted only in 3 cases, which amounted to 6%, respectively. Mild pain, which does not require taking analgesics, was observed in 34 (48.6%) patients in group I, while in group II it was observed in 20 (40%) patients. It should be noted that infertility was detected in 30% of cases and was found among women with a combined form of endometriosis and retro-cervical endometriosis who suffered from primary infertility. Thus, it should be noted that general clinical studies are the most important in making a diagnosis, since the results allow us to reliably assess the severity of the course of this disease.

#### EVALUATION OF COMBINATION THERAPY OF INOSITOLS, ANTIOXIDANTS AND VITAMINS IN POLYCYSTIC OVARIAN SYNDROME: A MULTICENTRIC RETROSPECTIVE OBSERVATIONAL STUDY (ROSE STUDY)

**Ekika Singh**<sup>26</sup>, Rekha Rajendra Kumar<sup>1</sup>, Nalina Devrajan<sup>2</sup>, Sona Ghosh<sup>3</sup>, Somya Sinha<sup>4</sup>, Swapnil Manglekar<sup>12</sup>, Sarika Zunzare<sup>8</sup>, Mona Dubey<sup>10</sup>, Pallavi Prasad<sup>15</sup>, Manisha Agrawal<sup>13</sup>, Deepa Sangole<sup>11</sup>, Aditi Singh<sup>16</sup>, Pratibha Rai<sup>19</sup>, Pratik Mawani<sup>14</sup>, Kirtan Vyas<sup>7</sup>, Shalini Garg<sup>9</sup>, Spandana Challagulla<sup>21</sup>, T. Surekha<sup>20</sup>, Nishu Singla<sup>6</sup>, Guduru Mydhili<sup>17</sup>, Satpal Kaur<sup>18</sup>, Chhaya Goyal<sup>5</sup>, Kartik Nakhate<sup>22</sup>, Sandesh Kamdi<sup>23</sup>, Lavanya C.<sup>24</sup>, Vanitha R.<sup>25</sup>

<sup>1</sup>Gynecology, Chandana Hospital & Miracle IVF Hospital, Bangalore, India

<sup>2</sup>Gynecology, NDR Hospital, Bangalore, India

<sup>3</sup>Gynecology, Rana Hospital, Gorakhpur, India

<sup>4</sup>Gynecology, Women's Clinic, Ranchi, India

<sup>5</sup>Gynecology, Heera Lal Hospital, Agra, India

<sup>6</sup>Gynecology, Singla Hospital, Bilaspur, India

<sup>7</sup>Gynecology, Sevak Maternity & Surgical Hospital, Ahmedabad, India

<sup>8</sup>Gynecology, Ankur Hospital, Nanded, India

<sup>9</sup>Gynecology, Sushil Garg Hospital, Karnal, India

<sup>10</sup>Gynecology, Dueby Clinic, Allahabad, India

<sup>11</sup>Gynecology, Dr Deepa Sangole's Clinic in Kalina, Mumbai, India

<sup>12</sup>Gynecology, Chintamani Hospital, Ratnagiri, India

<sup>13</sup>Gynecology, Satya Trauma and Maternity Center, Kanpur, India

<sup>14</sup>Gynecology, World Laparoscopy Hospital, Ahmedabad, India

<sup>15</sup>Gynecology, Prasad Polyclinic, Hyderabad, India

<sup>16</sup>Gynecology, Parmar Hospital, Gandhinagar, India

<sup>17</sup>Gynecology, Mydhili Hospital, Gudur, India

<sup>18</sup>Gynecology, Dr. Satpal Kaur Clinic, Ludhiana, India

<sup>19</sup>Gynecology, PMCH Hospital, Dhanbad, India

<sup>20</sup>Gynecology, Surekha Hospital, Rajamundry, India

<sup>21</sup>Gynecology, Jeevan Hospital, Hyderabad, India

<sup>22</sup>Pharmacology, Rungta College of Pharmacy, Bhilai, India

<sup>23</sup>Medical Services, Corona Remedies, Ahmedabad, India

<sup>24</sup>Gynecology, Malar Hospital, Trichy, India

<sup>25</sup>Gynecology, Coastal Hospital, Adyar, India

<sup>26</sup>Gynecology, Sharda Narayan Hospital, Mau, India

**Problem statement:** Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder which is rapidly gaining epidemic proportions in the world. Insulin resistance (IR) and oxidative stress are recognized as important contributing factors in the pathogenesis of PCOS. Different combinations of various insulin sensitizing agents, antioxidants and vitamins are available in the market but, there is scarcity of evidences pertaining to their efficacy and safety in PCOS patients. **Methods:** Multicentric retrospective observational cohort study was planned at twenty-five fertility and or gynaecological clinics in different states of India from April 2019 to February 2020. Both lean and obese patients (16-39 years; n=129) with confirmed diagnosis of PCOS as per the Rotterdam/ESHRE criteria were included in study. From the day of diagnosis of PCOS, patients were received a marketed formulation, Trazer F Forte™ containing insulin sensitising agents (inositols,

NAC and chromium), antioxidants (NAC and lycopene), and vitamins (vitamin D, biotin and folic acid) twice daily as a tablet for 3 to 6 months. Primary outcomes were improvements in signs of PCOS (menstrual cyclicity or ovulation restoration, acne and hirsutism), body weight, body mass index, waist circumference, ovarian cysts, pregnancy rate and hormonal balance. Secondary outcome was the evaluation of side effects. **Result:** Combination therapy of insulin sensitizers, antioxidants and vitamins showed significant improvement in menstrual cyclicity by 48.1% and 78.9% in obese PCOS cases, and 50% and 74.1% in lean PCOS cases after 3- and 6-month of intervention respectively. Significant improvement was observed in acne, hirsutism and ovarian cysts post-intervention in both obese and lean PCOS women. After successful completion of the treatment, significant corrections were observed in metabolic (fasting glucose, fasting insulin and HOMA-IR) and hormonal profile (free testosterone, LH:FSH ratio, AMH and progesterone) in obese as well as lean PCOS cases. The clinical pregnancy rate was 15.5% and 31.5% in obese women, and 7.5% and 20% in lean cases after 3- and 6-month of intervention respectively. **Conclusion:** Combination of inositols, antioxidants and vitamins can be used as a promising and clinically relevant non-hormonal treatment option for women with PCOS for satisfactory clinical outcomes.

**Disclosure of Interest:** None

#### A CASE OF FUMARATE HYDRATASE DEFICIENT UTERINE LEIOMYOMA ASSOCIATED WITH A RARE GENETIC DISORDER

**Payam Katebi Kashi**<sup>1</sup>, Katherine L. Dengler<sup>2</sup>

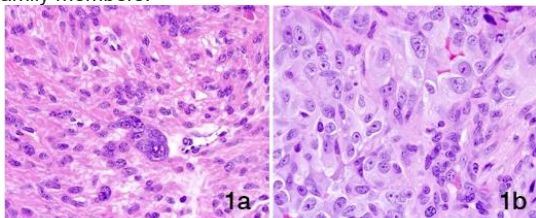
<sup>1</sup>Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Inova Fairfax Women's Hospital, Falls Church, USA

<sup>2</sup>Division of Urogynecology, Department of Obstetrics and Gynecology, Walter Reed National Military Medical Center, Falls Church, USA

**Problem Statement:** Fumarate hydratase (FH)-deficient leiomyomas can develop from somatic genetic alterations or as a manifestation of the autosomal dominant disorder hereditary leiomyomatosis and renal cell carcinoma (HLRCC). FH encodes fumarase, an enzyme that participates in the tricarboxylic acid cycle. The mechanism by which FH acts as a tumor suppressor is not fully understood, but other tricarboxylic acid cycle genes are known to act as tumor suppressors for other tumors, such as hereditary paragangliomas and succinate dehydrogenase. Affected individuals along with an increased risk of a distinct type of renal cell carcinoma can develop cutaneous leiomyomas and most women develop uterine leiomyomas. While it was originally thought that cutaneous leiomyomas were ubiquitous in this syndrome, subsequent reports suggest that cutaneous lesions are only present in less than one-half of affected individuals.

**Methods:** A 34 year-old female with menometrorrhagia was seen for symptomatic uterine leiomyomas. Her history was significant for alpha thalassaemia minor, anemia, gastroesophageal reflux disease, uterine leiomyoma, and morbid obesity with a body mass index of 41 kg/m<sup>2</sup>. Her transvaginal ultrasound was normal except for a large submucosal fundal leiomyoma measuring 12 x 11 x 4 centimeters. After counseling she opted to have an abdominal myomectomy via mini laparotomy. **Results:** A four centimeter pfannenstiell incision was used to access to pelvis and removed the leiomyoma. The uterus was repaired using barbed suture in multiple layers. The pathologic specimen weighed 350 grams with findings of uterine smooth muscle neoplasm composed of spindle cells in fascicles. There was focal moderate to marked atypia in some nuclei with eosinophilic nucleoli and alveolar halos. Additionally, staghorn vessels, eosinophilic cytoplasmic globules and an alveolar pattern of edema were seen. The findings were consistent with fumarate hydratase deficient leiomyoma with focal bizarre nuclei consistent with HLRCC

(Figure 1 a, b). **Conclusion:** Although most cases of uterine leiomyomas are benign, some unique cases are associated with specific genetic disorders. Knowledge of these disorders and their permutations can lead to prompt diagnosis. Pathologic reporting of a fumarate hydratase-deficient leiomyoma should prompt referral to a genetic counselor for risk evaluation of HLRCC in the individual and family members.



1a: Fumarate hydratase deficient leiomyoma with bizarre nuclei  
 1b: Focal moderate atypia with eosinophilic nucleoli and alveolar halos

## A STUDY ON THE EFFECT OF UTERINE ARTERY EMBOLIZATION

Il Dong Kim

Obstetrics and Gynecology, National Medical Center, Seoul, South Korea

**Problem statement:** Adenomyosis and uterine leiomyoma are common gynecological diseases that can cause symptoms such as menstrual irregularity, dysmenorrhea, increased uterine size, and infertility. In patients with uterine leiomyoma, uterine artery embolization is selected as a treatment method to maintain the uterus or to avoid surgical intervention. In general, hysterectomy and uterine myomectomy require general anesthesia, but uterine artery embolization is possible with conscious, partial anesthesia and a short recovery period, and is more cost effective. However, since the uterus is preserved after the procedure, the symptoms may continue. We here studied the effects of uterine artery embolization on uterine, myoma, and ovarian size as well as hemoglobin level before and after the procedure. **Methods:** We retrospectively reviewed the medical records of 30 patients who underwent uterine artery embolization from January 2010 to December 2018. Patients were divided into three groups: uterine leiomyoma, adenomyosis, and mixed leiomyoma and adenomyosis type. The changes in the uterine, myoma, and ovarian size and in the hemoglobin level were measured and compared before and 3 months after uterine artery embolization. Using medical records, the main symptoms of the patients before the treatment and the history of the treatment were examined. **Results:** One case of increased uterine size without response to treatment after uterine artery embolization showed a volume increase of 1.93%. After uterine artery embolization, her total uterine volume decreased by 42.82%. The right ovary showed an overall volume increase of 5.27%. The volume changes in the left ovary showed a 4.12% reduction overall. However, the bilateral ovarian volume was decreased in the leiomyoma group and was increased in the adenomyosis and mixed group. The hemoglobin changes in the blood increased by an average of 55.85% and was the largest in the mixed group. **Conclusion:** In this study, after uterine artery embolization, the size of the ovary did not change significantly. The procedure was effective in reducing the size of the uterus and the size of the myoma. Given that, increasingly, patients desire to preserve their uterus and want to return to their daily routine, uterine artery embolization is an appropriate option.

## QUALITY IMPROVEMENT STUDY FOR THE REDUCTION OF BLOOD TRANSFUSION POST GYNECOLOGICAL SURGERIES AT A CANADIAN COMMUNITY TEACHING HOSPITAL

Liyana Kukkadi<sup>1</sup>, Faye Dracopoulos<sup>2</sup>, Esther Cabrera<sup>3</sup>, Jennifer Cram<sup>4</sup>, Melissa Tai, Melissa Tai<sup>4</sup>

<sup>1</sup>School of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

<sup>2</sup>School of Medicine, University College Dublin, Dublin, Ireland

<sup>3</sup>Blood Management, Ontario Transfusion Coordinators, Toronto, Canada

<sup>4</sup>Department of Obstetrics and Gynecology, Michael Garron Hospital, Toronto, Canada

**Problem Statement:** According to Ontario Transfusion Coordinators (ONTraC) records in 2018, Michael Garron Hospital (MGH) ranked the highest amongst the twelve participant hospitals for blood product usage in elective gynecological surgeries. MGH's transfusion rate was 16.4% compared to the average rate of 8.1%. **Methods:** A case-series review of blood transfusions during major elective gynecological surgeries was conducted between 2016 and 2018. All possible factors associated with blood product use (such as age, medical comorbidities, surgical indications, surgical procedures, pathology, preoperative and postoperative hemoglobin levels, surgeon, and pre-operative iron usage) were examined. A cost comparison was completed to evaluate the difference in the cost of optimizing a patient's preoperative hemoglobin level with the price of administering one unit of packed red blood cells (PRBCs). **Results:** Eleven of twelve surgeons used blood products. Thirty-five patients required intraoperative and/or postoperative blood transfusions. The average age and BMI of the patients studied was 41 and 28.14, respectively. The patient population presented with few pre-operative morbidities; two in thirty-five had specified hemoglobinopathies. Transfusion occurred in cases indicated for fibroids and menorrhagia. Surgeries performed included total abdominal hysterectomies + adnexectomies and myomectomies. Nineteen patients had a length between preoperative assessment and surgery of greater than three weeks, providing enough time for sufficient preoperative hemoglobin optimization with intravenous iron. Twenty-six out of thirty-five patients had preoperative anemia (120 mg/mL) according to the World Health Organization standard. The completed cost analysis revealed a significant difference in cost between the administration of prophylactic intravenous iron and the use of postoperative and intraoperative blood products. The cost of transfusing blood is substantially higher for the hospital. **Conclusion:** A quality improvement strategy of adequate preoperative hemoglobin optimization with intravenous iron may lessen blood transfusion use and reduce costs for MGH. The use of tranexamic acid intraoperatively to reduce blood loss is a consideration for future studies.

## A NEW COMBINATION OF SOY ISOFLAVONES, 8-PN AND MELATONIN REDUCES SEVERE HOT FLASHES IN POSTMENOPAUSAL WOMEN WITH MODERATE-TO-SEVERE VASOMOTOR SYMPTOMS. A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

Francisco de Borja Caballero Borreda<sup>1</sup>, Maria Angeles Calleja Garcia<sup>2</sup>, Francisco Javier Lopez Moreno<sup>3</sup>, Syra Velasco Ortega<sup>4</sup>, Javier Leal Martinez-Bujanda<sup>4</sup>, Concepcion Nieto Magro<sup>4</sup>

<sup>1</sup>Department of Gynecology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain

<sup>2</sup>Gynecology, Consulta de Ginecología Dra. Angeles Calleja Garcia, Guadalajara, Spain

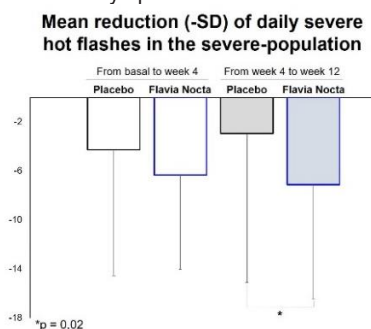
<sup>3</sup>Gynecology, Dr. Fco. Javier Lopez Moreno S.L., Madrid, Spain

<sup>4</sup>Medical Affairs, ITF Research Pharma S.L.U., Madrid, Spain

Abbreviations: 8-PN: 8-PrenylNaringenin

**Problem statement:** A rapid and large placebo-effect in postmenopausal women with moderate-to-severe vasomotor symptoms has been widely documented, hampering the proper evaluation of the efficacy of new clinical alternatives designed to manage these symptoms. Our study aims to demonstrate the safety and further efficacy of Flavia Nocta (a combination of 54mg of soy isoflavones –24.5mg of genistein–, 100µg of 8-PN and 1mg of melatonin, among other nutrients) in the clinical management of moderate-to-severe vasomotor symptoms.

**Methods:** We conducted a randomized, double-blind, placebo-controlled clinical trial in healthy postmenopausal women (n=104) with  $\geq 5$  moderate-to-severe hot flashes/day. Women took 1 capsule of Flavia Nocta (n=53) or placebo (n=51) per day, shortly before going to sleep, for 12 weeks. We studied the evolution of a subpopulation with the subjects who presented a higher proportion of severe hot flashes at week 4 (*severe-population*, n=46), in order to minimize the risk of including patients who had a rapid response and those who had a response primarily driven by mild-to-moderate hot flashes (which are likely to have good results due to the placebo-effect). The mean changes in the frequency of total and severe hot flashes at week 12 from each study visit in both populations were measured as efficacy endpoints. Safety assessment included adverse events evaluation. **Results:** Globally, a significant decrease in total and severe hot flashes frequency was achieved in both groups. Flavia Nocta reduced total hot flashes frequency by 36.8% and 56.6% and severe hot flashes frequency by 41.6% and 69.2% after 4 and 12 weeks respectively. Flavia Nocta had a better behavior than placebo within the *severe-population* group, achieving a greater reduction of severe hot flashes between weeks 4 to 12 (p=0.02). Flavia Nocta had remarkable safety results: only 1 patient presented an adverse event (influenza), not related to the product. **Conclusion:** Flavia Nocta achieved a clinically meaningful reduction of severe hot flashes in a more consistent and progressive fashion than placebo, especially within the *severe-population* where placebo-effect faded over time. Flavia Nocta has proven to be a safe and efficacious alternative for managing moderate-to-severe vasomotor symptoms.



#### THYROID ENLARGEMENT ASSOCIATED WITH ADMINISTRATION OF LONG-ACTING GONADOTROPHIN RELEASING HORMONE AGONIST IN MANAGEMENT OF A LARGE FIBROID

Shu Hui Lim, Yan Yan Celene Hui  
Obstetrics and Gynaecology, KK Women's & Children's Hospital, Singapore, Singapore

**Problem Statement:** Uterine fibroids are the most common benign tumours in women, and current management options include pharmacological treatment, surgery, as well as less invasive options such as high intensity focused ultrasound (HIFU) or uterine artery embolization. Gonadotrophin-releasing hormone (GNRH) agonists can be used to decrease fibroid volume, especially prior to surgery. Common side effects of GNRH agonist administration include hot flashes, irritability, breast

tenderness, and pain at injection site. There have been a few reports of thyroid disease associated with GNRH agonist administration.

**Case Presentation (Methods/Results):** A 43 year old lady presented to the gynaecologists with a history of rapidly increasing abdominal bloating, menorrhagia and urinary frequency secondary to a 13.3 x 12.8 x 9.2cm anterior fibroid. Her definitive hysterectomy was postponed during the COVID-19 pandemic. Hence, a single 11.25mg dose of intramuscular leuprolin acetate was administered as a temporizing measure for her symptoms. This successfully decreased fibroid volume by 27.5%, comparing radiological measurements of the fibroid on presentation with the measurements taken 2 months after the injection. 8 days after GNRH agonist administration, the patient visited the general practitioner complaining of a 5cm anterior neck mass. Thyroid ultrasound showed multiple thyroid nodules, but normal thyroid function. Anaesthetists assessed that she was fit for surgery, and she underwent an uncomplicated hysterectomy after COVID-19 restrictions were eased. She eventually also underwent left hemithyroidectomy 5 months after GNRH agonist administration in view of persistent globus sensation from the mass, and final histology demonstrated benign multinodular goiter. Thyroid function still remained normal prior to the hemithyroidectomy. **Conclusion:** The association between GNRH agonist and thyroid dysfunction is not well studied in literature, but limited case reports exist. It is postulated that fluctuations in serum gonadotropin and sex hormones induced by GNRH agonists may trigger thyroid dysfunction or aggravate underlying thyroid disease. This case report illustrates the relationship, and may suggest that clinicians screen for preexisting thyroid disease before administering GNRH agonists. However, more studies are required to prove a direct cause and effect relationship between GNRH agonists and thyroid disease.

#### PULMONARY BENIGN METASTASIZING LEIOMYOMA MIMETIZING SECONDARY MALIGN DISEASE: A CLINICAL CASE REPORT

Mariana Lira Morais, Sara Nunes, Prescillia Marques, Regina Severo, Herculano Martins, Zelia Gomes, Osvaldo Moutinho  
Gynecology/obstetrics, Centro Hospitalar Tras Os Montes E Alto Douro, Vila Real, Portugal

**Problem statement:** Uterine leiomyoma is the most common gynecological tumor. It rarely has benign extra-uterine growth patterns, including benign metastasizing leiomyoma (BML). The lung is the organ most frequently affected by BML. Pulmonary BML usually presents as numerous well defined nodules, some with cavitory or cystic features and they might be interpreted as a malignant disease. **Case Report:** We report a 49-year-old premenopausal woman, previously diagnosed with an invasive tongue squamous cell carcinoma in march of 2018. She had dyspnea on moderate exertion and a staging chest computerized tomography (CT) showed multiple bilateral lung nodules and cysts, possibly representing secondary malign disease. In April of 2018 she underwent right hemiglossectomy. She underwent a CT-guided percutaneous lung biopsy and the histological examination showed pulmonary parenchyma partially occupied by spindle cells arranged in short bundles, without atypia or mitotic activity. Immunohistochemically these cells contained smooth muscle specific actin. They also demonstrated positive immunoreactivity for estrogen and progesterone receptors. Subsequently, the patient was referred for gynecological evaluation. Transvaginal ultrasound revealed several myomatous nodules, the largest with 56x24mm. Abdomino-pelvic CT scan was performed that excluded other pelvic disease. She was diagnosed with BML associated with uterine leiomyoma. Total hysterectomy with bilateral annexectomy was

performed uneventfully, so as postoperative period. The histological study revealed uterine leiomyoma. Currently the patient continues to monitor pulmonary lesions through image studies and has had no exacerbation of BML. **Conclusion:** The diagnosis of BML remains challenging. Although rare in middle-age women, physicians should include BML in the differential diagnosis when presented with multiple pulmonary nodules associated with uterine pathology. Confirming smooth muscle origin with estrogen and progesterone receptor positivity via immunohistochemistry remains paramount to establishing the diagnosis. Given the rarity of the condition, there is no standardized treatment for BML. Current therapeutic options include expectant management and surveillance, hormonal frenation or oophorectomy.

## LAPAROSCOPIC TUBAL STERILIZATION AND REGRET

Matilde Martins<sup>1</sup>, Marcia Marinho<sup>2</sup>, Sara Cunha<sup>1</sup>, Carolina Carneiro<sup>1</sup>, Ines Reis<sup>1</sup>, Cristina Costa<sup>1</sup>, Teresa Teles<sup>1</sup>

<sup>1</sup>Obstetrics/Gynecology, Centro Hospitalar De Entre O Douro E Vouga, Santa Maria Da Feira, Portugal

<sup>2</sup>Obstetrics/Gynecology, Centro Hospitalar De Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

**Problem statement:** Female sterilization is the most common method of contraception worldwide, used by 19 per cent of women aged 15 to 49 years old. Although preoperative counseling should always address regret, little information is available about the proportion of patients who later regret the surgery, ranging from 1 to 26%. The purpose of this study is to evaluate the regret rate 5 years after a laparoscopic tubal sterilization and its reasons. **Methods:** A retrospective data analysis from all cases of laparoscopic bilateral tubal sterilization in our ambulatory surgery unit from July 2014 to December 2014 was conducted combining patient history at that time and a 5-year after the procedure phone call. **Results:** In 6 months, 118 laparoscopic bilateral tubal sterilization procedures by bipolar electrocoagulation were performed. 45 cases were excluded. Mean age and median parity were  $38,3 \pm 4.2$  and 2, respectively. 34,2% had history of caesarean section. The majority of patients were healthy (76,7%) and hypertension (15,1%) was the most frequent comorbidity associated. The estroprogestative combination was the previous contraceptive method more frequently used (73,97%), followed by no method in 10,9% and copper intrauterine device in 9,59%. Regret 5 years after the procedure was reported in 20,5% of women who had undergone tubal sterilization, being the most frequent reasons abnormal uterine bleeding (53,3%) and desire to have more children (40%). Although this desire, no patient demanded a medically assisted reproductive technique or tubal ligation reversal procedures. No failure cases were reported. **Conclusion:** Although our study has a considerable limitation (sample size), our findings showed that regret is relatively common among women who have undergone laparoscopic tubal sterilization (20,5%). The issue of relatively permanent fertility loss and risk of menstrual abnormalities should be discussed openly and clearly to women considering surgical sterilization as a permanent contraceptive method. No conflict of interest to declare.

## RAPID RATE OF GROWTH IN ADNEXAL MASSES, DESPITE BENIGN APPEARANCE ON ULTRASOUND, WAS ASSOCIATED WITH MALIGNANCY. A RETROSPECTIVE ANALYSIS OF 48 CONSECUTIVE CASES FROM A SINGLE INSTITUTION

Christina Moisisdis-Tesch<sup>1,2</sup>, Norman Ginsberg<sup>2</sup>

<sup>1</sup>Obstetrics and Gynecology, Obstetrics and Gynecology Group Practice in Medicum and St. Josefs Hospital, Wiesbaden, Germany

<sup>2</sup>Obstetrics and Gynecology, Association for Women's Health Care and Northwestern University Hospital, Chicago, USA

**Problem statement:** to compare the rate of malignancy in adnexal masses with benign appearance on ultrasound and low Risk of Malignancy Index (RMI) based on their rate of growth. **Methods:** All patients in our obstetrics and gynecology practice undergoing surgery between 2015 and 2020 for adnexal masses with only benign appearance on ultrasound according to IOTA simple rules were analyzed. Ultrasound findings of the adnexa up to 3 years prior to surgery, CA-125 levels and Risk of Malignancy Index were evaluated. **Results:** Patients ranged in age from 22 to 84; 27 were pre-menopausal and 21 were postmenopausal. All adnexal masses appeared benign on ultrasound using IOTA simple rules. CA-125 levels ranged from 4 to 127 U/mL. The Risk of Malignancy Index ranged from 7 to 127 and was never above 200 (indicative of malignancy). Ultrasound findings up to 3 years prior to surgery were available for 43 patients. In 39 of these patients, the adnexal mass was present and growing slowly over several months prior to surgery. The histopathology in these patients was benign. In the other 4 patients, the adnexal mass appeared to grow rapidly (defined as an increase in size by more than 50%, or first appearance in the 6-12 months prior to surgery) and all were found to have borderline or early stage ovarian or tubal carcinomas. The rate of malignancy was 9.3%. **Conclusion:** despite benign appearance on ultrasound and low Risk of Malignancy Index, adnexal masses with a rapid rate of growth were associated with a risk of malignancy of 9.3%. This finding warrants further study and may be useful in the planning of surgery for adnexal masses. *Disclosure of Interest:* The authors have no financial / commercial conflict of interests to report.

## PARASITIC FIBROIDS, THE RARE VARIANT

Silvia Morales Munoz, Natalia Sanchez Baudo, Esmeralda Lopez Lopez

Obstetricia Y Ginecologia, Hospital De Poniente, El Ejido, Spain

Uterine fibroids are the most common benign tumors in women. The parasitic myomas is a rare variant of myoma, classically defined as subserosal pedicled fibroma that is partially or totally detached from the uterus and ends up receiving its vascularization through a neovascularization coming from the tissues adjacent organs. We present the clinical case of a 39-year-old patient who consults in our service for heavy menstrual bleeding and sterility of 1 year of evolution. No medical-surgical history of interest. On examination, a tumoral formation is observed that reaches the umbilical level. In the transvaginal ultrasound, a uterus of 94x69 was observed with several intramural myomas of 3 and 4 cm and a subserous one in the background of 14cm. The resonance confirms the presence of a practically pedunculated myoma of 12x10 cm that reaches the height of the vertebral body L5. During laparotomy, a large fibroid with a fine avascular pedicle is observed and joined to the Omento by a variegated, multiple, serpentine and large caliber vascularization (up to 1 cm in diameter). The pathological anatomy describes a benign leiomyoma of 1140 gr. When a subserous myoma requires a blood supply greater than that provided by the uterus, it begins to receive it from neighboring structures, such as: Omento, Common Iliac Artery and the inferior Mesenteric artery. Its connection with the uterus diminishes partially and even totally, becoming then what is known as parasite myoma, cataloged by FIGO as type 8 myomas. Most of the published cases were diagnosed intraoperatively. Currently there has been an increase in this type of myoma that appears in an iatrogenic manner after surgery with morcellation. The spontaneous form is more rare and arises after twisting or progressive separation of the uterine pedicle to the myoma.

### PHASE 3, PROSPECTIVE, RANDOMIZED, PLACEBO-CONTROLLED, DELAYED TREATMENT, DOUBLE-BLIND STUDY TO EVALUATE EFFECTIVENESS AND SAFETY OF SINGLE-DOSE ORAL SECNIDAZOLE 2 GRAMS FOR TREATMENT OF TRICHOMONIASIS IN WOMEN

Christina Muzny<sup>1</sup>, Paul Nyirjesy<sup>3</sup>, **Greg Kaufman**<sup>4</sup>, Steven Chavoustie<sup>2</sup>, Jane Schwebke<sup>1</sup>

<sup>1</sup>Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, USA

<sup>2</sup>Department of Obstetrics and Gynecology, University of Miami Miller School of Medicine, Miami, USA

<sup>3</sup>Department of Obstetrics and Gynecology, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, USA

<sup>4</sup>Medical Affairs, Lupin Pharmaceuticals, Inc., Baltimore, USA

**Problem statement:** Trichomoniasis is the most prevalent non-viral sexually transmitted infection (STI) in the world, affecting 3.7 million people in the United States (US). It is associated with vaginitis and increased risk of HIV and other STIs. In addition, it can cause infertility and increase a woman's risk for adverse birth outcomes. The objective of this study was to evaluate the efficacy and safety of single-dose secnidazole 2g oral granules in women with trichomoniasis. Secnidazole is FDA-approved for the treatment of bacterial vaginosis in adult women. **Methods:** Subjects with a diagnosis of trichomoniasis (by wet mount, OSOM rapid test, and/or nucleic acid amplification test [NAAT]) were enrolled at a baseline visit (visit 1). Diagnosis of trichomoniasis was confirmed by a positive InPouch™ culture. At visit 1, subjects were also tested for chlamydia and gonorrhea by NAAT and randomly assigned in a 1:1 ratio to either secnidazole or placebo. They were evaluated for test-of-cure (TOC) by culture at visit 2 (days 6–12), at which time they received the opposite treatment from enrollment (i.e., active treatment if they received placebo at baseline or placebo if they received active treatment at baseline). They were followed at subsequent visits for resolution of trichomoniasis and need for additional therapy. The primary efficacy endpoint was microbiological cure (i.e., InPouch™ culture negative for *T. vaginalis*) at TOC visit. **Results:** 147 women were enrolled at 10 sites. The modified intent-to-treat (mITT) population included 131 randomized subjects who were culture positive for *T. vaginalis* and negative for gonorrhea and chlamydia at baseline. The primary efficacy endpoint in the mITT population was 92.2% (59/64) for secnidazole versus 1.5% (1/67) for placebo ( $P = 0.001$ ). In the per-protocol population, the cure rate was 94.9% (56/59) for secnidazole versus 1.7% (1/60) for placebo ( $P = 0.001$ ). Secnidazole was well tolerated with the most commonly reported adverse events being vulvovaginal candidiasis (2.7%) and nausea (2.7%). No serious adverse events were observed. **Conclusion:** Secnidazole 2g single dose had significantly improved clinical efficacy and safety compared to placebo. The high degree of efficacy (92%–95%) supports this drug's role in treating women with trichomoniasis.

### SELF-TREATMENT HABITS IN WOMEN PRESENTING SYMPTOMS AND SIGNS OF VULVOVAGINITIS

Ana Rosa Masero Casasola<sup>1</sup>, Jesus Lazaro-Carrasco de la Fuente<sup>2</sup>, Syra Velasco Ortega<sup>3</sup>, **Maria Palma Santisteban**<sup>3</sup>

Concepcion Nieto Magro<sup>3</sup>

<sup>1</sup>Gynecology, Clinica Centrosur, Madrid, Spain

<sup>2</sup>Gynecology, Centro Medico Arpa Medica, Madrid, Spain

<sup>3</sup>Medical Affairs, ITF Research S.L.U., Madrid, Spain

**Problem statement:** Signs and symptoms of infectious and non-infectious vulvovaginitis are often similar, including pruritus, increased vaginal discharge, erythema and edema. Similarities between different conditions cause confusion in women who suffered previous episodes, leading to self-treatment habits. A significant number of women self-diagnose and self-treat based on earlier

experiences without proven infection. Inappropriate treatment of uncomplicated infections can affect the ecological characteristics of pathogenic agents and worsen the outcome of infections, resulting in an increased incidence of recurrences, mixed infections and appearance of resistant strains. **Methods:** An observational, transversal, multicenter clinical study included 103 women with symptoms and signs of vulvovaginitis were diagnosed and treated based on the physician's clinical practice. Vaginal exudate sample was collected for microbiological culture in all patients. Self-treatment habits were evaluated through questionnaire specifically asking about the type of product used for the current episode before attending the office. Vaginal samples were also evaluated. **Results:** Results showed that 32(31.1%) women in this study had used a pharmacological and/or non-pharmacological alternative to self-treat their current episode. 27 pharmacological products were used, mainly antifungals (20/27). Most popular non-pharmacological measures were intimate hygiene solutions(12) and probiotics(6). Microbiological results were negative in 12/32 and positive in 20/32 women. *Candida spp.* was present in 16(80%) samples and *G.vaginalis* in 2(10%) samples. 75% of women who had used antifungals to self-treat the current episode tested positive for pathogenic agents. 1 of 2 women that used treatment for bacterial vaginosis tested positive in vaginal exudate. **Conclusion:** A significant number of women in the study had self-treated their current episode, however, all of them still presented symptomatology and many of them still tested positive in the exudate. This may suggest that the chosen self-treatment measures might not be the most adequate options for their particular condition, hence the importance of visiting the doctor to be properly advised, diagnosed and treated. As for self-treatment options, non-pharmacological alternatives like probiotics and intimate hygiene solutions, may be helpful choices to manage vaginal disturbances since they are not aimed for specific target pathogens being suitable for vulvovaginitis of diverse etiology, without risking a contribution to future complications.

### PREVALENCE AND MICROBIOLOGICAL CHARACTERIZATION OF VAGINAL MIXED INFECTIONS AMONG WOMEN WITH SYMPTOMS AND SIGNS OF INFECTIOUS VULVOVAGINITIS

Francisca Ridocci Pallares<sup>1</sup>, Ana Rosa Masero Casasola<sup>2</sup>, **Maria Palma Santisteban**<sup>3</sup>, Syra Velasco Ortega<sup>3</sup>, Concepcion Nieto Magro<sup>3</sup>

<sup>1</sup>Gynecology, RyD Consulta Materno Infantil, Valencia, Spain

<sup>2</sup>Gynecology, Clinica Centrosur, Madrid, Spain

<sup>3</sup>Medical Affairs, ITF Research Pharma S.L.U., Madrid, Spain

**Problem statement:** Mixed vaginitis is defined as the simultaneous presence of at least two different vaginal pathogens, both contributing to an abnormal vaginal milieu leading to vaginal signs and symptoms. Increasing incidence of these infections poses a clinical and therapeutic challenge. Infectious vulvovaginitis is often diagnosed based on clinical history, gynecological examination and symptom discussion, hence, empirical treatment is frequently prescribed lacking confirmation of the definitive diagnosis on the specific infective agents. **Methods:** An observational, transversal, multicenter study was performed including 103 women who attended the gynecologist's office presenting symptoms and signs of infectious vulvovaginitis. Women were diagnosed and prescribed a treatment based on the physician's usual clinical practice. A vaginal exudate sample was collected for culture to confirm microbiological diagnosis. Prevalence of vaginal mixed infections, pathogens involved and agreement between clinical and microbiological diagnosis were evaluated. **Results:** Among these 103 women, 6 mixed infections were suspected clinically. Microbiological analysis identified 10 mixed infections in the whole sample:

in 90% of them *Candida spp.* was present. Agents responsible for mixed infections included 7 *C. albicans* + *Gardnerella*; 1 *C. glabrata* + *Gardnerella*; 1 *C. albicans* + *Gardnerella* + *Streptococcus Agalactiae* (B) and 1 *Saccharomyces cerevisiae* + *Gardnerella*. Among these 10 cases, only one had been diagnosed clinically. Microbiological diagnosis confirmed the presence of 47 women with *Candida spp.* (44 cases of *C. albicans* and 3 of *C. glabrata*), being the most prevalent infection in the studied women. Most of these candida infections involved a single agent, however 19.14% of them (9 cases) were vaginal mixed infections. **Conclusion:** Mixed vaginal infections are prevalent among women with symptoms and signs of vulvovaginal infection. Correct diagnosis represents a challenge for physicians, in order to select the most appropriate treatment to solve the episode and avoid further complications. A large majority of them involve *Candida*. Vulvovaginal candidiasis is a very frequent condition, commonly associated with bacterial infections. While clinical identification of these mixed infections appears poor, prescription of antifungals with a broad spectrum of antimycotic and antimicrobial activity is an adequate choice in the therapeutic approach of women with symptoms of vulvovaginal candidiasis.

#### A CASE OF DISSEMINATED PERITONEAL LEIOMYOMATOSIS AFTER ABDOMINAL HYSTERECTOMY WITHOUT MORCELLATION

**Mariana Doria**, Ana Mesquita Varejao, Mafalda Laranjo, Catarina Peixinho, Rita Sequeira Campos, Claudio Rebelo  
*Gynecology and Obstetrics, Pedro Hispano Hospital, Matosinhos, Portugal*

**Problem Statement:** Disseminated Peritoneal Leiomyomatosis (DPL) is a rare benign entity (prevalence 1:1.000.000), which predominantly affects women during their reproductive years. It is characterized by the dissemination of multiple smooth muscle nodules along the peritoneal surfaces. The patients are usually asymptomatic, with diagnosis being incidental. Pathophysiology is not fully understood, but hormonal, genetic and/or iatrogenic causes have been proposed. Most cases occur in women with history of uterine morcellation in laparoscopic procedures. Although this disease is benign, the risk of malignant transformation is 2 to 5%. **Methods:** A case report of DPL. **Results:** We report a case of a 53-year-old asymptomatic woman referred to our department after an incidental finding of pelvic nodules in routine pelvic examination. Two years before she had total abdominal hysterectomy without morcellation for symptomatic fibroids (uterine bleeding and severe anaemia). Abdominopelvic magnetic resonance imaging showed confluent peritoneal smooth muscle-like nodules, measuring a total of 98x60x80 mm. The patient underwent an exploratory laparotomy, which revealed a cluster of grey-red lesions, measuring approximately 100 mm, involving the right adnexal area, peritoneum, right pelvic wall and Douglas' Pouch. There was no ascites or lymph node enlargement. Resection of the nodules and bilateral oophorectomy were performed, without complications. Histological findings confirmed the hypothesis of DPL, showing multiple nodules weighing 140 grams in total, the biggest one measuring 75x53x40mm. The postoperative period was uneventful. A follow up abdominopelvic ultrasound 6 months after surgery revealed no evidence of recurrent or residual masses. **Conclusion:** The interest of this case relies on its rarity and the fact that most cases described in literature are associated with uterine morcellation in laparoscopic procedures. This patient had a conventional abdominal hysterectomy by laparotomy 2 years before. DPL, although rare, should be included as a differential diagnosis in women with a history of hysterectomy or myomectomy and the diagnosis of pelvic masses. Its diagnosis can be difficult preoperatively, as it resembles peritoneal and ovarian carcinoma or metastasis.

For this reason, surgical excision is normally performed for pathological diagnosis. Recent articles showed that aromatase inhibitors can also play a role, especially for recurrences after surgery.



#### USING GOOGLE TRENDS TO DETERMINE SEASONAL VARIATION IN MENOPAUSE SEARCH AND ITS CORRELATION WITH DEPRESSION SEARCH TRENDS

**Chris Andrea Robert<sup>1</sup>**, Mary Phyllis Robert<sup>2</sup>, Kathy Amy Robert<sup>3</sup>

<sup>1</sup>OBG, Sunrise Hospital, Solapur, India

<sup>2</sup>OBG, Lih Hospital, Abu Dhabi, United Arab Emirates

<sup>3</sup>OBG, Bangalore Fetal Medicine Centre, Bangalore, India

**Objective:** To determine seasonal variation in internet information-seeking behavior for menopause and ascertain if a correlation between menopause and depression search trends exists. **design:** Retrospective search analysis using Google Trends. **Materials and methods:** We utilized Google Trends to query the term 'menopause' globally over the period from 2004 to 2020. The seasonality of search trends for 'menopause' was examined using this data. We then compared it to the term 'depression' and studied for a correlation between the pair. **Results:** Menopause often negatively influences the quality of life of a patient. Because of its non-urgent nature, patients frequently turn to the internet as a medium of information. Search trends is on an increasing trend from 2011 onwards. Using the one-way ANOVA test, there was a statistically significant difference in the search query for the word 'menopause' between the months (p-value 0.01). When the search results were averaged for each month, the most number of searches were observed in August; furthermore, there was a decline in November and December. The top related queries for menopause were 'menopause symptoms,' 'after menopause,' and 'menopause age.' In the US, the states with the most considerable number of queries on menopause were Maine, New Hampshire, New York, West Virginia, and North Carolina. During the transition to menopause, patients additionally may be at a higher risk of depression. When the association between the search terms 'menopause' and 'depression' was probed, it showed a high correlation exists in search trends between the two variables using the Pearson correlation coefficient (0.646), which was statistically significant with a p-value of 0.01. **Conclusions:** Google trend is a beneficial tool to analyze the patient information-seeking behavior. There seems to be an increasing trend in search behavior over the years and also a seasonal fluctuation in the search behavior with August averaging higher and November and December averaging lower than the other months in the search trends for the word 'Menopause'. Though there seems to be a significant correlation between menopause and depression, caution must be used to interpret this data as demographic data cannot be gleaned off google trends.

## ENDOMETRIAL PATHOLOGY IN PERIMENOPAUSE ASSOCIATED WITH METABOLIC SYNDROME

**Aneta Sima**, Drage Dabeski, Slagana Simeonova Krstevska, Ana Daneva Markova, Sofija Zlateska, Arta Bina Gynecology, Endocrinology, University Clinic of Obstetrics/Gynecology- Skopje, North Macedonia, Skopje, Republic of North Macedonia

**Abstract Introduction:** Perimenopause as a clinical entity is characterized by a series of symptoms that occur due to the initial estrogen deficiency of multiple organs and systems. The most common are changes in the endometrial mucosa (hyperplasia, fibroids, endometrial polyps, malignant changes). Metabolic syndrome is an entity composed of a group of risk factors that increase the risk of cardiovascular disease. According to the American National Heart Academy, AHA, the diagnosis is confirmed if the patient has 3 of the following symptoms: ↑ waist circumference (88 cm), ↑ triglyceride level (2 mmol/l), ↓ HDL level cholesterol, high blood pressure (above 130/85 mmHg), elevated glucose levels (5.5 mmol/l). Menopause is an independent risk factor, with a tendency to worsen with age. The prevalence reaches up to 60% in the postmenopausal period. **Objectives:** The aim of this study was to detect pathology of the endometrium in perimenopause, to determine whether there is a metabolic syndrome and risk factors, as well as the association between them. **Material and methods:** This was a prospective cohort study, performed at the University Clinic of Ob/Gyn, from 2017-2018. 100 patients with abnormal uterine bleeding in the perimenopause were included, aged 45-50 years, divided into two groups according to BMI: a) first group - BMI up to 30 (increased body weight), b) second group - BMI 30 (obese patients), c) control group (40) - asymptomatic patients. Gynecological examination was performed, followed by fractional curettage in both groups with abnormal bleeding. Blood pressure, glycaemia, lipid status, waist circumference, waist / hip ratio, BMI were also analyzed. **Results:** Endometrial hyperplasia was found in 50% of patients, polyps in 30%, myomas and deficient endometrium in 20%. Hyperglycaemia was observed, increased BMI over 30 kg/m<sup>2</sup>, high blood pressure, abdominal obesity. The prevalence of metabolic syndrome in the first group is 80.3%, in the second 41.2% and in the third group is 17.5%. **Conclusion:** Endometrial hyperplasia has increased incidence in perimenopause, also with an increased risk of metabolic syndrome and strong association between them. Menopause requires multidisciplinary approach.

## PREVALENCE AND RISK FACTORS OF COEXISTING ENDOMETRIOSIS IN WOMEN UNDERGOING LAPAROSCOPIC MYOMECTOMY FOR SYMPTOMATIC LEIOMYOMA AND SUBFERTILITY

Natalya Danilyants, Paul MacKoul, Louise van der Does, Marysa MacKoul, Nilofar Kazi  
Research, The Center for Innovative GYN Care, Rockville, USA

**Problem statement:** In women undergoing laparoscopic myomectomy, a diagnosis of concomitant endometriosis should not be overlooked, as both conditions contribute to dysmenorrhea, dyspareunia, and subfertility. The objective of the current study was to explore the prevalence and risk factors for the coexistence of uterine leiomyoma and endometriosis during laparoscopic-assisted myomectomy. **Methods:** Retrospective case series of 390 patients who underwent laparoscopic-assisted myomectomy at an ambulatory surgery center by 2 high-volume surgeons between October 3, 2018 – June 3, 2020. The coexistence of endometriosis and uterine leiomyoma was confirmed via postoperative pathology. This study was deemed exempt according to 45 CFR 46.101(b) by IntegReview IRB, an independent institutional review board. **Results:** Histology-proven endometriosis was found on pathology in 45.4%

cases of women undergoing laparoscopic myomectomy. Nulliparous women were more likely to have concomitant endometriosis (91% v 78%; p=.001). While the average number of fibroids did not vary between groups, the average total fibroid weight (253 g v 547 g; p=.000) and average length of largest fibroid (6.9 cm v 9.3 cm; p=.001) were significantly larger in the group without endometriosis. **Conclusion:** Coexistence rate of leiomyoma and endometriosis is not well understood. Previous literature reports the coexistence during laparoscopic myomectomy is between 12%-26%. But our prevalence rate was much higher; histologic confirmation of concomitant endometriosis was 45.4%. As both conditions are estrogen dependent and have overlapping symptoms, surgeons are strongly encouraged to thoroughly inspect and biopsy the pelvic cavity for endometriosis in women undergoing myomectomy, particularly in patients with subfertility, as studies show leiomyoma is rarely the only cause of infertility. Failing to remove endometriotic lesions during myomectomy may lead to continued pain, suboptimal treatment of fertility (including potentially wasted time and money on IVF treatments), and eventual reoperation. As high-volume, surgical specialists, our coexistence rate may be attributed in part to population bias; however, given histologic confirmation of endometriosis in almost half our myomectomy patients, the surgical treatment of leiomyomas and endometriosis warrants further exploration. **Disclosure/Conflict of Interest:** None

Patient Characteristics and Operative Findings			
Variable (Mean)	Patients with endometriosis N=177	Patients without endometriosis N=213	p value
Age, yr	36.5 (4.8)	37.4 (6.4)	.208
BMI, kg/m <sup>2</sup>	25.3 (6.4)	28.9 (6.6)	.000
Nulliparity	91.0	77.9	.001
Race			.089
Black	46.3	55.9	
White	17.5	11.3	
Asian	10.2	4.2	
Other	9.0	8.4	
Previous Abdominal/Pelvic Surgery	53.1	53.5	.187
Avg. Total fibroid weight, g	252.8 (259.5) (1.1-1180)	547.4 (688.5) (2.6750)	.000
Avg. Number of Fibroids	6.8 (7.5) (1-40)	9.8 (11.9) (1-59)	.071
Avg. Length of largest fibroid, cm	6.9 (3.9) (1.8-20)	9.3 (5.6) (1.7-42)	.001
Location of fibroids			
Anterior	33.9	30.5	.272
Posterior	35.0	33.8	.441
Fundal	22.0	23.9	.416
Fallopian tubes	20.9	26.8	.157
Lateral	27.7	31.0	.505
Myoma Type			
Intramural	54.2	68.1	.006
Submucosal	58.8	59.6	.918
Subserosal	31.6	38.5	.168
Pedunculated	28.2	38.5	.041
Concomitant Adenomyosis on Pathology	19.2	14.1	.216

Data are given as mean (SD) or as percentage; Chi-square significance test

## BENIGN LESION IN A RARE LOCATION: A CASE REPORT OF A VULVAR LEIOMYOMA

Juhannah Lynn Vano

Obstetrics and Gynecology, University of Santo Tomas Hospital, Manila, Philippines

Leiomyomas whose growth is other than the uterus is rare. It accounts for 0.03% of all gynecologic neoplasms and 0.07% of vulvar tumors. There are only 160 cases of vulvar leiomyomas reported in literature, and there are no published cases from the Philippines. We discuss a rare case of vulvar leiomyoma in a 41-year-old G1P1 (1001) presenting with a 13-year history of a right labial mass. Patient underwent excision of the mass with repair of the labial excess skin to provide optimal cosmetic post-operative results. The study was performed according to the CARE guidelines for case reports.

## IS THERE AN HRT PRESCRIBING PROBLEM?

Agata Zielinska<sup>1</sup>, Laith Alexander<sup>2</sup>

<sup>1</sup>Academic Foundation Programme, Imperial College Healthcare NHS Trust, London, UK, London, UK

<sup>2</sup>Academic Foundation Programme, Guys and St Thomas NHS Foundation Trust, London, UK, London, UK

**Problem statement:** Hormone Replacement Therapy (HRT) is prescribed to alleviate climacteric symptoms and comes with risks. One the major risks is associated with unopposed oestrogen, which in women with a uterus increases the risk of endometrial hyperplasia and cancer. Whilst comprehensive guidelines exist, the complexity of HRT prescribing and UK's recent HRT stock shortages could increase the risk of prescribing errors. We aimed to identify the number of women exposed to unopposed oestrogen due to incorrect HRT use. **Methods:** In one primary care practice in Suffolk, UK, we carried out an automated search to identify women taking oestrogen-only HRT prescriptions without a coded hysterectomy or intrauterine system (IUS) in-situ, resulting in unopposed oestrogen exposure. We manually evaluated their notes to check for uncoded hysterectomies or IUSs. All women identified as incorrectly receiving unopposed oestrogen were followed up, a new template for HRT prescribing was introduced and prescribing errors were re-evaluated following 6 months. **Results:** 31 women (of 218 taking HRT) were initially identified as having potential exposure to unopposed oestrogen. By manually evaluating their notes, we found that five women with a uterus were being exposed to unopposed oestrogen with durations ranging between 10-30 months; an error rate of 2.3%. Reasons for errors included miscommunication between doctors and nurses, confusion over HRT trade names and inadequate documentation of IUS insertion and expiry dates. When we introduced a new prescribing template and re-audited prescriptions six months later, the number of women incorrectly receiving oestrogen-only HRT had fallen to zero. **Conclusion:** An incorrect unopposed oestrogen exposure rate of 2.3% among this population could mean that thousands of women in the UK are taking oestrogen-only HRT when they should be taking combined HRT. It is important to ensure fail-safe systems when prescribing HRT, because prescribing errors can increase the risk of endometrial cancer. Simple interventions, including the rigorous use of formalised, regularly updated templates coupled with frequent practitioner training could go some way to minimising these errors. **Competing interests:** None declared.

## HPV

### DISTRIBUTION OF HIGH-RISK HUMAN PAPILLOMAVIRUS GENOTYPES AMONG KAZAKHSTANI WOMEN

Aisha Babi<sup>1</sup>, Torgyn Issa<sup>1</sup>, Chee Kai Chan<sup>1</sup>, Azliyati Azizan<sup>1</sup>, Raushan Alibekova<sup>1</sup>, Saleem Khan<sup>2</sup>, Alpamyss Issanov<sup>1</sup>, Gulzhanat Aimagambetova<sup>1</sup>

<sup>1</sup>Department of Biomedical Sciences, Nazarbayev University School of Medicine, Astana, Kazakhstan

<sup>2</sup>Department of Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, Pittsburgh, USA

**Problem statement:** Human papillomavirus (HPV) represents a great burden for the health of Kazakhstani women. However, little is known about HPV prevalence in Kazakhstan. The aims of this study were to genotype HPV DNA in cervical swab samples to determine the prevalence of HPV genotypes around the country, and to identify the differences between regions. **Methods:** Cervical swab samples were collected from women attending gynaecological clinics at five Kazakhstan cities (Nur-Sultan, Almaty, Aktobe, Pavlodar, and Oskemen), representing different parts of the country. In total, 890 women aged between 18 and 70 participated in the study. Samples were genotyped using real-time multiplex PCR with an Amplisense HPV genotyping kit. **Results:** HPV testing showed that 774 (86.97%) women attending gynaecological clinics were positive for HPV infection. The greatest proportion of HPV positive women were in Nur-Sultan (23.51%), Almaty (23.39%), and Aktobe (21.32%).

There was no statistical difference in HPV prevalence between the regions ( $p=0.468$ ). Among HPV positive women, high-risk HPV type 16 was the most prevalent (82.13%). The rest of HPV types had a prevalence of less than 6%. Around 65% of HPV infected women had only one HPV genotype and almost 16% of women were co-infected with 2 HPV genotypes. Less than 1 % of women were co-infected with either 5 or 6 genotypes. **Conclusion:** This study reveals a high prevalence of HPV infection among women attending gynaecological clinics in Kazakhstan. Together with strengthening the knowledge about HPV prevalence in Kazakhstan, the study results can contribute to health policy development and decision-making about HPV vaccination and cervical cancer prevention. **Disclosure of Interest:** This study was supported by the Nazarbayev University Grant Number is 110119FD4528, 2019-2021.

### IS THE RISK OF RESIDUAL CIN RELATED TO MARGEN STATUS AND HPV AFTER LEEP?

Natalia Del Valle Sanchez Baudo, Morales Munoz Silvia, Lopez Lopez Esmeralda  
Obstetricia Y Ginecologia, Hospital De Poniente, Almeria, Spain

**Context:** Loop ectrosurgical excision procedure (LEEP) is a basic procedure in the ionization performed on patients with CIN II/III. After treatment, close follow up is esencial for the earlier detection of residual and recurrent disease. **Problem statement:** To evaluate the performance of the "immediately posttreatment HPV testing" and "margin status" in detecting residual or recurrent disease after LEEP for cervical intraepithelial neoplasia. **Methods:** The study was based in 'Hospital de Poniente' (Almeria, Spain) and it enrolled women during their follow-up period for cervical lesions induced by HPV. 61 patients were involved in the survey for whom epithelial cell anomalies were detected at cervical biopsy and then LEEP procedures were performed. All patiennts were followed up with PAP-smear and colposcopy after 4-6 months posttreatment. HPV was performed at the time of LEEP and repeated 4-6 month later. **Results:** A "negative margin status" and a "negative immediately posttreatment HPV testing" demonstrated a negative predictive value (NPV) of 0,89 and 0,93 respectively as predictor of "no recurrence of dysplasia". On the contrary, a "positive margin status" and a "positive immediately posttreatment HPV testing" demonstrated a positive predictive value (PPV) 0,25 y 0,1 respectively, so they are not good markers of risk or recurrence of cervical dysplasia. **Conclusions:** The combined evaluation of the Immediately posttreatment HPV testing and surgical margin status could allow to subdivide patients treated with LEEP into categories at different risk of cervical dysplasia recurrence.

## OTHER

### PERIPARTUM CARDIOMYOPATHY: AN AUSTRALIAN CASE REPORT

Oltana Agastra, Rebecca Yuan Li, Roberto Orefice  
Obstetrics and Gynaecology, The Canberra Hospital, Canberra, Australia

**Background:** Peripartum cardiomyopathy (PPCM) is a rare condition that develops antenatally or in the early post-partum period (1). It has an unknown pathogenicity and presents with clinical signs and symptoms of heart failure. The incidence varies among different regions, with an incidence estimated at between one in 900 and one in 4000 live births in the United States (1). Little is known about the incidence of PPCM in Australia (2). This case study aims to add to the limited literature about PPCM in Australia. **Case report:** A 33-year-old primigravida, primipara woman presented day 10 post-partum to the Emergency Department with a 2-day history of dyspnoea, orthopnoea

and shortness of breath on exertion. She also complained of a dry cough and had a history of gradually increasing peripheral lower limb oedema. On examination, she was tachycardic and saturating at 94% on room air. Heart sounds were dual with no murmur and there were basal crackles on auscultation of the chest. She also had bilateral peripheral pitting oedema up to the knees. Bedside echocardiogram showed globally reduced ventricular function with a small pericardial effusion. She was admitted to the Coronary Care Unit for continuous telemetry. Transthoracic echocardiogram revealed severe left ventricular dilatation with severe global systolic dysfunction and an ejection fraction of 20-25%. Based on this, she was diagnosed with PPCM. She was commenced on Bisoprolol, Perindopril and Furosemide, and commenced on a 1.2-1.5L fluid restriction. She was discharged on day five of her admission with planned Cardiology follow up. She was followed up by the cardiology team in June 2020, and had a repeat echocardiogram showing an ejection fraction of 30% as well as ongoing severe global impairment of systolic function. **Discussion:** There are significant implications for subsequent pregnancies for women who have had PPCM. Women with persistently reduced left ventricular ejection fraction have a high risk of heart failure and mortality, and still births and preterm births are more common in women with persistent left ventricular dysfunction (3,4). Given these consequences, it is crucial to consider the diagnosis of PPCM in women presenting with symptoms of heart failure.

#### PERSISTENT PREGNANCY OF UNKNOWN LOCATION, DILEMMAS IN MANAGEMENT

**Shailaja Anipindi**, Hannah Ajayi, Alexander Field  
*Obstetrics and Gynaecology, Princess Alexandra Hospital, Harlow, Essex, UK*

**Problem statement:** Persistent pregnancy of unknown location (PPUL) remains a controversial clinical problem with no consensus on diagnosis or management. The final diagnosis of PPUL accounts for 3% of the initial diagnosis of Pregnancy of Unknown location (PUL). PPULs behave biochemically like ectopic pregnancies and may represent ultrasonically missed ectopic pregnancies. PPUL is defined as greater than three serial serum human chorionic gonadotropin (hCG) levels that change 15% while the location of pregnancy remains unclear on transvaginal ultrasound. The time frame is not clear to guide clinicians the appropriate time of intervention. We therefore sought to find out what constitutes a PPUL and their final outcomes. **Methods:** A retrospective audit of all cases of PUL was done and the final outcomes were defined and analysed in terms of the time to diagnosis and the final management. **Results:** The time to diagnosis (ttd) was calculated as the time from the first scan to the time when the final outcomes were reached. The ttd for PPUL was 28 days, whereas for the other outcomes such as failing PUL, intrauterine pregnancy and ectopic pregnancy, it was around 14-16 days. The median initial hCG was 180IU/L and the range was 60-1574IU/ml. Management options included laparoscopy and uterine curettage, methotrexate and expectant management. There were five negative laparoscopies and chorionic villi were not identified in two of them. One was managed expectantly with bhcg and the other had Methotrexate due to plateauing hCG levels. **Conclusion:** PPUL is a diagnosis of exclusion. The final diagnosis can be determined only after uterine curettage based on the presence or absence of chorionic villi. But it is not recommended for every case of PPUL. As per our data, majority of the cases of PPUL could be safely managed with either Methotrexate or expectant management. A few case reports of persistently elevated hCG levels associated with gestational trophoblastic neoplasia have been reported. So, it is safer to follow-up PULs until they have a negative pregnancy test to avoid misdiagnosis.

#### THYROID ANTIBODIES AND MATERNAL AND NEONATAL REPERCUSSIONS IN PREGNANCY

**Sufia Athar**, Zeena Martis, Mohammad Alloub, Jacqueline Alipoon Ongsip, April Kristine Hernandez Cedero  
*Obstetrics and Gynecology, Hamad Medical Corporation, Al Wakra, Qatar*

**Problem statement:** Amongst the common endocrinological disorders of pregnancy, thyroid disorders rank second after diabetes. Thyroid autoimmunity is linked to sub-fertility, miscarriages, preterm birth, gestational diabetes and adverse neurodevelopmental sequelae in children. There is paucity of research in the gulf countries in this regard. Our study was conducted to assess the effects of thyroid antibodies on adverse maternal and neonatal outcomes in pregnancy. **Methods:** A Retrospective study chart review was conducted at a Secondary Hospital in Qatar. Records of the women who delivered in 2017 to June 2018 were evaluated. Prevalence of hypothyroidism was assessed. 400 patients were selected by simple random sampling. The study population was divided in three groups: Group A – Hypothyroid in pregnancy with antibodies, Group B Hypothyroid in pregnancy without antibodies and group C – Euthyroid in pregnancy. Maternal and neonatal outcomes were compared. Odd's ratio was evaluated using Medical online software. **Results:** The prevalence of hypothyroidism in the study population was 3.47% in the study population. 33.33% hypothyroid patients had thyroid antibodies. Patients with thyroid peroxidase (TPO) antibody and those with both TPO and Thyroglobulin antibodies were 33.33% and 4.44% respectively. Patient with more than one miscarriage were 30% (OR 2.059, 95%CI-1.112 to 3.811, P = 0.0215), 21.24 % (OR-1.196, 95%CI- 0.676 to 2.115, P = 0.537) and 17% in group A, B and C respectively. Gestational diabetes was noted in 32 % in Euthyroid patients, 41.7% % (OR-1.3021, 95%CI-0.755-2.245, P=0.3424), and 35.6 % (OR-1.112, 95%CI-0.708-1.746, P=0.6436) in group A and B. The incidence of preterm births was 10% (OR- 2.22, 95%CI- 0.7603 to 6.4951, P = 0.1445), 4.23 % (OR- 0.9416, 95%CI- 0.308 to 2.876, P = 0.9159) and 4.5% in groups A, B and C respectively. Small for dates babies were 10 % (OR-3.33, 95%CI-1.0368-10.71, p=0.0433), 5.93 (OR-1.9774, 95%CI-0.64-6.0237, p=0.23), and 3 % in groups A, B and C respectively. The study revealed positive correlation between thyroid antibodies and adverse maternal and neonatal outcomes in pregnancy. **Conclusion:** Thyroid antibodies are associated with adverse maternal and neonatal outcomes in pregnancy. **Disclosure of Interest:** none

#### CRITICAL ANALYSIS OF MATERNAL RISK FACTORS AND OBSTETRIC BACKGROUND AND CARE OF MOTHERS OF NEWBORNS REQUIRING NEONATAL INTENSIVE CARE UNIT ADMISSION DUE TO BIRTH ASPHYXIA

**Indranil Banerjee**<sup>1</sup>, Sudip Bain<sup>2</sup>, Gargi Mukherjee<sup>1</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Basildon and Thurrock University Hospitals, Basildon, UK

<sup>2</sup>Obstetrics and Gynaecology, Ashoknagar State General Hospitals, Ashoknagar, India

**Problem statement:** Birth asphyxia depends on maternal and fetal risk factors. Early identification of high-risk factors with improved antenatal and intrapartum care can decrease birth asphyxia rate. **Methods:** It was retrospective cross-sectional study, conducted at department of obstetrics and gynaecology, MMCH. Study was conducted from March, 2019 to February, 2020 with estimated sample size was 80. The study was done after approval by institutional ethics committee. Data were collected from respective mothers and analysed by SPSS19. **Results:** In our study, total number of mothers was 80. Mean maternal age of babies born with asphyxia was found to be 23.86 years. Majority of mothers were belong to lower socio-economic status

(68.75%). Birth asphyxia was more common in unbooked mothers (52.50%), primipara (51.25%) and in term pregnancy (75%). It was found that birth asphyxia significantly more common in presence of maternal or fetal risk factors than absence of maternal and fetal risk factors. Maternal antepartum and intrapartum risk factors were anaemia (40%), augmentation by oxytocin (36.25%), prolonged second stage of labour (31.25%), prolonged rupture of membrane (26.25%), PIH or preeclampsia and eclampsia (26.25%), maternal fever (11.25%), history of IUFD (10%) etc. Fetal risk factors were meconium stained liquor (25%), prematurity (23.75%), breech presentation (22.50%), twin pregnancy (15%), IUGR, cord prolapse. Birth asphyxia rate was more common in caesarean section (53.75%) delivery, low birth weight and male babies. **Conclusions:** It was found that low socioeconomic status and particularly some risk factors during pregnancy and parturition e.g. maternal anaemia, PIH, injudicious use of oxytocin, meconium stained amniotic fluid, prolonged second stage of labour, prolonged rupture of membrane, low birth weight babies were associated with higher incidence of birth asphyxia. So early identification of the potential maternal and fetal risk factors and proper care may reduce the burden of birth asphyxia as well as its consequences.

#### A RARE CASE OF PUERPERAL PSYCHOSIS PRECEDING FORMAL DIAGNOSIS OF SCHIZOPHRENIA

Kawthar Barkat, Rebecca Li

Obstetrics and Gynaecology, The Canberra Hospital, Canberra, Australia

**Objective:** Puerperal psychosis (PP) is a life-threatening psychiatric emergency characterised by paranoia, depression, mania, hallucinations, delusions 1,2,3. It affects 0.1% of deliveries with onset within four weeks postpartum 3. Pre-disposing factors include previous psychiatric disorders, family history, limited social support, hormonal imbalance, insomnia 3,4,5. Half of women with PP history experience a recurrent episode 6,7. Urgent hospitalisation, psychotherapy, antipsychotic/mood-stabiliser administration, and electroconvulsive therapy mitigate maternal suicide and infanticide 8,9,10. Here, we describe a case of severe PP that unconventionally preceded a formal diagnosis of schizophrenia. **Case Report:** A 24-year-old G3P2 woman with non-English speaking background, limited antenatal care, and no psychiatric history delivered a female infant and discharged within 24 hours. She declined any history, examination, or intervention throughout her admission. Antenatally, she rejected an Edinburgh Depression Score and did not disclose any underlying mental health concerns. She had two previous uncomplicated vaginal births. She immigrated to Australia in 2013 and is separated from her children's father. She re-presented three weeks post-partum with agitation, paranoia, and delusional thought content; believing her neighbours were poisoning her. She verbally confronted them and threatened physical assault. The patient lacked insight, declined assistance, and attempted abscondence, thus necessitating legally mandated emergency detention. She received olanzapine and lorazepam with good effect. She continually expressed breastmilk for her baby who did not develop side-effects. Child Protective Services supported her children while she was hospitalised. She engaged well with psychotherapy, social work, and Perinatal Mental Health Services. She was formally diagnosed with schizophrenia prior to discharge following seventeen days of inpatient management. She received fortnightly domiciliary visits and depot olanzapine until she re-located city. The patient will seek psychiatric assistance for future pregnancies due to PP recurrence risk. **Discussion:** PP presents with mood and psychotic symptoms with potentially fatal outcomes 8,10. Rarely does

PP precede formal diagnosis of schizophrenia as described in this case. This highlights the importance of stringent antenatal mental health screening for underlying risk factors to judiciously implement protective measures. PP requires rapid diagnosis, hospitalisation, multidisciplinary input, and antipsychotic/mood-stabilising medications 8,9. These interventions are particularly poignant for non-English speaking mothers with limited social support 4. (Full references on poster)

#### A CASE OF VIRILISATION SECONDARY TO ANDROGEN-SECRETING OVARIAN TUMOUR IN A POSTMENOPAUSAL WOMAN

Kawthar Barkat, Sumi Saha

Obstetrics and Gynaecology, The Canberra Hospital, Canberra, Australia

**Objective:** Benign or malignant androgen-producing ovarian tumours in postmenopausal women are rare but potentially life-threatening (1,2). They clinically manifest with severe virilisation characterised by masculinisation, alopecia, and hirsutism (2). Other differential diagnoses for postmenopausal androgen-excess include iatrogenic factors, polycystic ovarian syndrome, hyperthecosis, obesity-induced hyperandrogenic anovulation, Cushing's syndrome, and Congenital Adrenal Hyperplasia (1). Identifying and treating the underlying aetiology prevents the cardio-metabolic sequelae of hyperandrogenemia. Here, we report a successfully managed case of virilisation secondary to androgen-secreting ovarian tumour in a postmenopausal woman. **Case Report:** A 64-year-old postmenopausal woman presented with rapidly progressing androgenic alopecia characterised by 75% loss of scalp hair. It was associated with severe hirsutism of the face, chest, abdomen, and back as well as unintentional weightloss. The multiparous patient had Class 3 Obesity, Type 2 Diabetes Mellitus, and underwent subtotal hysterectomy at 37 years of age secondary to debilitating menorrhagia - she received no oestrogen post-hysterectomy. Initial hormonal evaluation showed elevated serum testosterone (8nmol/L) and SHBG (47.8nmol/L). She had normal DHEA-S, FAL, prolactin, cortisol, and thyroid function levels. Androgen-secreting malignancy of endocrine or ovarian origin was suspected. Computed tomographic scan demonstrated a large lesion suspicious of a solid nodule involving her left ovary. A right adnexal cystic mass was also visualised with no right ovary identified. Transvaginal ultrasound scan yielded similar findings. Laparoscopic bilateral salpingo-oophorectomy was performed. Extensive adhesions with Pouch of Douglas obliteration were noted intraoperatively. Histopathology demonstrated bilateral small benign inclusion cysts of the ovaries, no fallopian tube atypia, and no malignancy. Six weeks post-operatively, her plasma testosterone levels normalised with regression of clinical symptoms. **Discussion:** Virilisation in postmenopausal women may uncover an androgen-secreting ovarian tumour - a rare but potentially life-threatening diagnosis (1,2). This case highlights the importance of prompt clinical recognition, thorough investigation, and urgent intervention to improve quality of life and prevent significant morbidity and mortality. This is particularly poignant as our aging population surges and additional cases of postmenopausal hyperandrogenism emerge (2). Full references on poster : 1. Rothman, 2011

2. Markopoulos et al., 2015

#### AGENDA EUROPE V. THE MADRID DECLARATION: CLASH OF ULTRA-CONSERVATISM AND LIBERALISM IN GYNECOLOGICAL CLINICS

Jan Gregus

Center for Outpatient Gynecology and Primary Care, Brno, Czech Republic

Center for Prenatal Diagnosis, Brno, Czech Republic

**Problem statement:** A spectre is haunting Europe: the spectre of ultra-conservatism. The most conservative, traditionalist Christian groups have united into a single body called Agenda Europe, a pan-European, ultra-conservative Christian network that organizes an annual non-public summit in different European capitals. Its manifesto, "Restoring the Natural Order," details a worldview that aims to rewind sexual and reproductive freedoms in all European countries, and specifically for certain categories of people including women, adolescents, and the LGBTQ+ community. In answer, the European Society of Contraception and Reproductive Health released a position paper known as The Madrid Declaration. **Methods:** This presentation is based on analysis of "Restoring the Natural Order" and other Agenda Europe documents, as well as of the Madrid Declaration and other documents concerning human rights. **Results:** The Manifesto serves as a guideline for rolling back the progress achieved in LGBTQ+ and women's rights regarding free choice, including restrictions on abortion, contraception, assisted reproduction, comprehensive sexuality education and divorce. In contrast, The Madrid Declaration highlights the fact that sexual and reproductive health are integral human rights. It defends evidence-based medicine and the importance of making contraception available throughout Europe. Underlining the importance of comprehensive sexuality education with a focus on marginalized populations, it calls for access to legal and safe abortion, infertility treatments, and STD prevention and therapy. **Conclusion:** Criminalizing abortion, prostitution, same-sex relationships, etc. means punishing deeply personal decisions with a negative effect on sexual and reproductive health. It also undermines liberal democracy based on tolerance, human rights and secular laws. The threats to democracy often target the rights of women and minorities first. Metaphorically speaking, the clash of ultra-conservative and liberal forces over the future of Europe is currently raging in gynecology clinics. For this reason, gynecologists should familiarize themselves with the existence of such networks. Christians should be concerned that fringe parts of their communities claim to speak on behalf of all Christians. *I have no financial relationships to disclose.*

#### THE RELATIONSHIPS BETWEEN SOCIODEMOGRAPHIC CHARACTERISTICS AND ATTITUDES TO INDUCED ABORTION FOLLOWING DEFECTS DETECTED IN THE FETUS

Keren Grinberg

Nursing, Ruppin Academic Center, Emek-Hefer, Israel

**Problem statement:** Induced or artificial abortion is an elective termination of pregnancy for reasons such as unwanted pregnancy or detected birth defects in the fetus. Abortions and the related moral dilemmas are as old as time, and are common worldwide. This issue has medical, psychological, social, moral, political, legal and religious aspects, but few studies have examined the factors that affect public attitudes to abortions. **Methods:** This study examined the attitudes of the general population in Israel to abortions related to detected fetal defects and diseases, by means of a questionnaire distributed to 161 respondents aged 18-65. **Results:** The results showed that the more religious respondents were, the more negative their attitude to induced abortions was. Economic status also affected attitudes, so that people with a higher than average income had a more positive attitude than people with a lower income. No differences were found between Jews and non-Jews, or various levels of education. **Conclusion:** Medical staff should be given various ways to deal with this issue such as approaching the patient, increasing awareness of fetal defects and their implications, opening support centers

for couples and women, and increasing awareness of the sensitivity and difficulty of making these painful decisions.

#### WHEN PARANGANGLIOMA DISGUISES AS SEVERE PRE-ECLAMPSIA: A CASE REPORT

Mauli Jhala<sup>1</sup>, Gregory Jenkins<sup>1</sup>, Surjit Tarafdar<sup>2,3</sup>

<sup>1</sup>Obstetrics and Gynaecology, Westmead Hospital, Sydney, Australia

<sup>2</sup>Renal Medicine, Blacktown Hospital, Sydney, Australia

<sup>3</sup>Medicine, Western Sydney University, Sydney, Australia

**Problem Statement:** A 38-year-old female presented for the birth of her second child (gravida 2, parity 2) and had a severe perioperative hypertensive emergency during a routine lower segment caesarean section. The patient was known to have a history of pre-eclampsia in both her pregnancies and gestational diabetes in this pregnancy.

**Methods:** Antepartum, the patient developed pre-eclampsia at 38 weeks and was commenced on Labetalol. Peri-operatively, she needed to be managed with a hydralazine infusion and magnesium sulphate due to severe hypertension. She required further administration of multiple antihypertensive agents intra-operatively to stabilise her blood pressure. The patient was investigated for secondary hypertension with serum and urine catecholamines and CT angiogram. Following delivery, she was discharged on labetalol and nifedipine, with a plan to follow up in an outpatient clinic for review of her blood, urine and imaging results. **Results:** The patient's serum and urine catecholamine levels were significantly elevated. CT angiogram revealed a highly vascular enhancing solid mass left of the descending aorta and medial to left kidney, consistent with a retroperitoneal paraganglioma. This mass was further evaluated with a PET scan, which confirmed a large heterogenous left retroperitoneal soft tissue mass. She underwent laparoscopic removal of the left retroperitoneal paraganglioma. Postpartum her blood pressure was stable on a combination of alpha and beta blockers.

**Conclusion:** Paragangliomas and pheochromocytomas are neural crest cell derived neoplasms that are rare catecholamine producing tumours. Pheochromocytomas are limited to tumours that originate from the adrenal medulla. Similar tumours that originate from other sites including extra adrenal tumours, such as this patient had, are referred to as paragangliomas. Paraganglioma and its diagnosis in pregnancy is often delayed, as clinical symptoms can mimic those of pre-eclampsia or gestational hypertension. Although extremely rare, it can be a life-threatening medical condition for a mother and her foetus, with maternal morbidity rates as high as 50%. While hypertension is the most prominent sign, other signs and symptoms can be nonspecific. In this case, investigation and differential diagnosis of persistent hypertension led to the rare finding of paraganglioma.

#### INTRAVENOUS IMMUNOGLOBULIN THERAPY (IVIG) AND RHESUS DISEASE IN PREGNANCY

Rohadarshine Mahenthiran, Roberto Orefice

Department of Obstetrics & Gynaecology, The Canberra Hospital, Canberra, Australia

**Problem statement:** Rhesus (RH) isoimmunization is a condition leading to haemolytic disease of the newborn (HDN) via transplacental transfer of maternal antibodies that actively attack paternal Rh antigens within infant circulation causing hemolysis [1]. Consequentially, there are risks of intrauterine anaemia leading to further varying degrees of jaundice and anaemia post birth. It is suggested that IVIG therapy inhibits the production of maternal antibodies and partially blocks transplacental antibody channelling [3]. There has been success reported with antenatal immunoglobulin therapy with a reduction in rates of exchange transfusions, umbilical catheter requirements

and neurological impact [2,4]. Does IVIG therapy improve pregnancy outcomes in Rhesus disease in pregnancy?  
**Methods:** A case series discussing the pregnancy outcomes of six multiparous women identified with pregnancies affected by Rhesus disease where IVIG was commenced. The measured outcomes include gestation at delivery, birth weight, highest serum bilirubin, transfusion requirements and severity of disease. Verbal and written consents were obtained prior to presenting these data.  
**Results:** Overall, we have seen positive outcomes with IVIG reflected by a decrease for need for blood transfusion in three cases and no requirement in one case. Meanwhile in two cases, the requirement was unchanged from the first pregnancy. Birth weights improved in three cases and unchanged in one. However, in two cases, there was a drop in birth weights. Two cases showed decreased length of stay in the NICU while another two cases showed unchanged duration of NICU stay. In terms of the highest SBR recorded, there was an improvement seen in two cases, unchanged in one and an increase in two. In four cases, the gestation at delivery was improved. **Conclusion:** IVIG significantly reduces transfusion requirements, improves birth weights and prolongs pregnancy. A larger study is imperative to further support these findings and the use of IVIG in managing Rhesus disease in pregnancy.

#### VASECTOMY - A NEGLECTED METHOD OF EFFECTIVE CONTRACEPTION

Gargi Mukherjee

Obstetrics and Gynaecology, Basildon and Thurrock University Hospitals, Basildon, UK

**Problem statement:** Vasectomy, the permanent sterilisation in men, is a safe, quick, cheap and effective way of contraception. However, in a country like India, the acceptance of vasectomy is lagging far behind its female counterpart, sterilisation. **Methods:** The study was carried out in Calcutta National Medical College, a tertiary care hospital in India from August 2010 to July 2012. Male partners of a couple who has completed the family (□ 2 children) included in the study after informed consent. The technique followed was No Scalpel Vasectomy (NSV) which was done in the outpatient setting under local anaesthesia. Average time of the procedure was 10 minutes and the patients were discharged home on the same day with oral antibiotics. They were advised to come for follow up after 3 months with a repeat semen analysis. In between additional barrier contraception was supplied. **Results:** Among 1360 people who were consented for the procedure, 24 (1.76%) dropped out. Comparison between vasectomy and tubal sterilisation showed vasectomy : tubectomy ratio 1 : 1.7 . Though the national ratio of vasectomy: tubectomy in India is 1: 37 , but the in-depth counselling by a dedicated team managed to convince them. The prevailing misconceptions were increased risks of cancer and heart disease , weakening effect on overall health by the procedure. The complication rate was low, commonest were pain (1.19%), Infection (2.02%) and swelling (0.97%) 842 (63%) of the clients returned back after 3 months and repeat semen analysis revealed successful operation in all the cases. Another 359 clients returned back within 1 year of procedure and there has not been any report of failure yet. **Conclusion:** This simple and safe method needs to be popularized. Despite increase in contraception practice and couple protection rate in India, acceptance of vasectomy has not increased significantly compared to tubectomy which is a more complicated procedure. Counselling through mass media and access to good quality service may help to popularize the method.

#### AN AUDIT ON REDUCED FETAL MOVEMENT

Gargi Mukherjee

Obstetrics and Gynaecology, Basildon and Thurrock University Hospitals, Basildon, UK

**Problem statement:** Reduced fetal movement (RFM) is an element of Saving Baby Lives Care Bundle initiative of RCOG. An annual audit was undertaken to ascertain areas of non-compliance and improvement. **Method:** The retrospective audit was undertaken in Basildon and Thurrock University Hospitals in the Obstetrics and Gynaecology department. 40 sets of health care records were selected where women presented in triage with the complain of reduced fetal movement in the month of September to November 2019. Relevant history taking and evaluation of risk factors, clinical examination , auscultation(28 weeks) or CTG (28 weeks) were performed and were managed according to the results. **Results:** Among all the patients presented with reduced fetal movement, 80% were more than 28 weeks, 90% presented with the first episode, 70% presented with reduced fetal movement only, 77.5% of them had no risk factors. 5% had GDM, 5% had BMI35 , 2.5% has H/O SGA, 2.5% had low PAPP, 5% was smoker, 2.5% had IUGR in this pregnancy. The Fetal heart was auscultated and had a CTG in all cases appropriate for the gestation. Documentation of AC/EFW was done in all USS. RFM leaflet was provided in all patients. Documentation to return back if RFM recurs was done in all patients who were discharged. 97.5% were appropriately managed in accordance with the guidance. One patient was asked to return back for a CTG even after criteria met and patient was reassured with fetal movements. 27.5% were induced for RFM. Among the 12 patients induced for RFM, 9 had no CTG concerns, 1 was suspicious and 1 pathological CTG. 57.5% had a vaginal delivery, 12.5% had instrumental delivery. Among the 30% of caesarean section, only 5% was due to CTG concerns. 100% was livebirth. **Conclusion:** Reduced fetal movement being a subjective complaint, is difficult to treat. But studies have shown that 55% of women who had stillbirth experienced preceding reduced fetal movement. Thus it is very important to appropriately manage the patient who present with reduced fetal movement which was achieved in this audit.

#### COMPARISON OF PREGNANCY RISKS AMONGST DIFFERENT HEALTHCARE PROFESSIONALS

Oliver O'Brien, Ciara Reynolds, Eimer O'Malley, Emma Tuthill, Sharon Sheehan, Michael Turner

UCD Centre for Human Reproduction, Coombe Women and Infants University Hospital, Dublin, Ireland

**Problem Statement:** The last generation has seen major demographic changes in the medical profession in Ireland. About half of recent graduates are female, many are graduate entrants to medicine and for career reasons many are deferring motherhood. The purpose of this observational study was to compare pregnancy risks in medical doctors with that in other healthcare professionals who delivered in a large Irish maternity unit. **Methods:** The study was confined to all women who delivered a baby weighing 499g in the nine years 2008-17. Clinical and sociodemographic data was computerised as part of the hospital records by a trained midwife at the first antenatal visit and updated after delivery. Maternal occupation was self-reported. **Results:** Of the 66,828 women, 563 (0.8%) were medical doctors, 3,246 (4.8%) were nurses and 871 (1.3%) were other healthcare professionals (HCPs). The characteristics of the study population are shown in Table 1. The first column of p values is from the comparison of doctors with nurses, while the second is from the comparison of doctors with HCPs. Compared with nurses, doctors were more likely to be 30 years old and to be nulliparous and less likely to be obese and have an

unplanned pregnancy. Doctors were less likely to have gestational diabetes than nurses (5.3% vs 12.5%,  $p=0.001$ ) but not HCPs (3.9%). 71% of doctors took pre-pregnancy folic acid supplementation. Compared with HCPs, doctors were more likely to be obese and have an unplanned pregnancy. There were no differences between the three groups in mean birthweight, neonatal admissions, preterm delivery or emergency caesarean section (CS) rate. The elective CS rate in doctors was higher than in HCPs (22.0% vs 15.4%,  $p=0.001$ ) but not compared with nurses. Doctors were more likely to exclusively breastfeed than nurses (58.0% vs 46.1%,  $p=0.001$ ) but not HCPs (61.5%).

**Conclusion:** Despite studying obstetrics and neonatology as part of their undergraduate education, medical doctors have high pregnancy risks such as advancing age and poor breastfeeding rates. With regard to pre-conception folic acid, overweight/obesity and breastfeeding, they compare positively to nurses but less favourably to other HCPs and there is significant potential for improvement.

Table 1. Characteristics based on maternal occupation category.

	Doctor <i>n</i> = 563	Nurse <i>n</i> = 3246	<i>p</i> - value	HCP <i>n</i> = 871	<i>p</i> - value
Age (mean, SD)	34.8 (4.2)	33.8 (4.0)	<0.001	34.2 (3.5)	0.010
Age < 30 years (%)	9.6	14.5	<0.001	7.6	NS
Nulliparas (%)	39.1	33.9	0.008	43.1	NS
Irish born (%)	61.1	59.3	NS	82.4	<0.001
Unplanned pregnancy (%)	11.9	18.9	<0.001	8.0	0.007
BMI (median, IQR)	23.7 (4.6)	24.7 (5.3)	<0.001	22.5 (3.7)	<0.001
Underweight (%)	1.8	1.5	NS	1.7	NS
Normal weight (%)	60.2	51.8	<0.001	76.0	<0.001
Overweight (%)	26.8	32.5	0.003	17.2	<0.001
Obesity (%)	11.2	14.3	0.026	5.1	<0.001
Postconceptional folic acid only (%)	27.0	39.9	<0.001	18.4	<0.001
Preconceptional folic acid (%)	71.0	59.0	<0.001	81.0	<0.001
Feeding intention; breastfeeding (%)	95.4	87.6	<0.001	91.9	0.005
Depression (%)	0.7	0.6	NA	0.2	NA
Anxiety (%)	0.7	1.4	NA	1.7	NA
Anxiolytics/antidepressants (%)	1.1	1.0	NS	0.9	NS
Smoked previously (%)	12.1	26.1	<0.001	25.1	<0.001
Smoked in pregnancy (%)	0.2	1.9	NA	0.7	NA
Alcohol before pregnancy (%)	59.0	47.3	<0.001	73.1	<0.001
Alcohol use in pregnancy (%)	2.3	0.9	0.002	2.1	NS
Illicit drugs before pregnancy (%)	0.5	1.0	NA	1.7	NA
Illicit drugs in pregnancy (%)	0.0	0.2	NA	0.1	NA

NS – Not significant. NA – Numbers too small for statistical analysis.

HCP – Healthcare Professional. BMI – Body Mass Index.

## MOTHER AND EARTH; POLYAROMATIC HYDROCARBONS AND INTRAUTERINE GROWTH RESTRICTION

Kate van Berkel

Obstetrics and Gynaecology, Royal Women's Hospital, Parkville, Australia

College of Arts and Social Sciences, Australian National University, Canberra, Australia

Polyaromatic hydrocarbons (PAH), compounds produced by burning fossil fuels, are becoming increasingly notorious for their ill effects on health. An expanding body of research has linked these PAHs to pathological impacts on growth of babies within the womb known as intrauterine growth restriction (IUGR). A mammoth number of people, predominantly in the developing world, are experiencing high levels of PAH exposure due to the burning of fossil fuels for cooking and other domestic work, and ambient PAH exposure from increasing numbers of motor vehicles. The significant sequelae of IUGR mean the impact of PAHs has far-reaching and deeply damaging implications. The emerging research in this area belongs to a new field of scientific inquiry known as planetary health, which aims to study human societies and their inter-relationship with the natural environment. The importance of planetary health cannot be understated, and whilst organisations such as the World Health Organisation are endeavouring to improve air quality around the world, further targeted research into the links between PAHs and IUGR is needed to enable a better start to life for billions of people who remain at risk.





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# LASER COURSE - VAGINAL ERBIUM LASER FOR WOMEN'S HEALTH

THURSDAY, NOVEMBER 19, 2020



14:00-16:45	HALL II
Short Course Description:	<p>Course participants will learn the basic principles of using lasers for a variety of minimally invasive non-surgical and surgical gynecology procedures.</p> <p>The course program consists of twelve topics divided into three parts: Part I covers the use of FotonaSmooth® Erbium laser systems in pelvic floor dysfunction indications and aesthetic gynecology. Part II is composed of short presentations of innovative new applications like the treatment of vulvar lesions and vaginal and urinary infections, while Part III is dedicated to a Q&amp;A session and end-of-course exam.</p> <p>Upon completing the end-of-course exam, participants will receive a Course Certificate.</p>
14:00-14:03	<p>Introduction</p> <p><b>Zdenko Vizintin, Slovenia</b></p>
	<b>Part I</b>
14:03-14:35	<p>Overview of vaginal erbium laser technology</p> <p><b>Zdenko Vizintin, Slovenia</b></p>
14:35-14:43	<p>Laser use in stress urinary incontinence (Intra-urethral approach)</p> <p><b>Adrian Gaspar, Argentina/USA</b></p>
14:43-14:54	<p>Laser use for treatment of vaginal laxity and pelvic organ prolapses</p> <p><b>Aleksandra Novakov-Mikic, Serbia</b></p>
14:54-15:07	<p>Laser treatment of Genitourinary Syndrome of menopause</p> <p><b>Marco Gambacciani, Italy</b></p>
15:07-15:21	<p>Laser treatments in aesthetic gynecology</p> <p><b>Jorge Gaviria, Venezuela/USA</b></p>
	<b>Part II</b>
15:21-15:27	<p>Laser treatment of vulvar lesions</p> <p><b>Alessandro Ghelardi, Italy</b></p>
15:27-15:35	<p>Laser treatment of episiotomy related complaints</p> <p><b>Aleksandra Novakov-Mikic, Serbia</b></p>
15:35-15:40	<p>Laser treatment of candidiasis</p> <p><b>Adrian Gaspar, Argentina/USA</b></p>
15:40-15:50	<p>Laser treatment of urinary tract infections</p> <p><b>James Zhang, China</b></p>

15:50-15:57	Vaginal delivery post laser treatment <b>Irena Hreljac</b> , <i>Slovenia</i>
	<b>Part III</b>
15:57-16:30	<b>Q&amp;A session</b> <b>Marco Gambacciani</b> , <i>Italy</i> <b>Aleksandra Novakov-Mikic</b> , <i>Serbia</i> <b>Irena Hreljac</b> , <i>Slovenia</i> <b>Neza Koron</b> , <i>Slovenia</i> <b>Zdenko Vizintin</b> , <i>Slovenia</i>
16:30-16:45	<b>End-of-Course Test</b>

## THE NEW NORMAL REQUIRES A NEW MINDSET: CHALLENGING MEDICAL LIMITS TO ART TREATMENT ACCESS

THURSDAY, NOVEMBER 19, 2020



<b>14:20-15:20</b>	<b>HALL I</b>
Chairperson	<b>Scott Nelson</b> , <i>UK</i>
	40 is the new 30 <b>Jacky Nizard</b> , <i>France</i>
	50 is the new 40 <b>Nick Macklon</b> , <i>UK</i>
	The same shape does not fit for everyone <b>Diana Alecsandru</b> , <i>Spain</i>

## PROBIOTIC SUPPLEMENTATION DURING PREGNANCY

THURSDAY, NOVEMBER 19, 2020

**BioGaia®**

<b>15:20-15:50</b>	<b>HALL I</b>
15:20-15:50	Probiotic supplementation during pregnancy. The role of <i>L. reuteri</i> strains in maternal health and in the development on the infant microbiota <b>Flavia Indrio</b> , <i>Italy</i>



## NEW APPROACHES TO OPTIMIZE ART OUTCOMES

FRIDAY, NOVEMBER 20, 2020



GEDEON RICHTER

12:30-13:30	HALL I
Chairperson	<b>Samir Hamamah</b> , <i>France</i>
12:30-12:50	Luteal phase support in ART: Individualization of progesterone treatment according to the type of cycle <b>Elena Labarta</b> , <i>Spain</i>
12:50-13:10	Predicting live birth probability at each step of the ART process via machine learning <b>Veronika Grzegorzczak Martin</b> , <i>France</i>
13:10-13:30	Receptivity window with a transcriptomic approach to improves outcomes <b>Samir Hamamah</b> , <i>France</i>

## UNSOLVED PROBLEMS IN WOMEN'S REPRODUCTIVE HEALTH

(Supported by Gedeon Richter - Hungary)

FRIDAY, NOVEMBER 20, 2020



GEDEON RICHTER

14:05-15:05	HALL II
Chairperson	<b>Georg Griesinger</b> , <i>Germany</i>
14:05-14:20	Diagnostic and therapeutic challenges of recurrent vulvovaginal candida infections <b>Gilbert G.G. Donders</b> , <i>Belgium</i>
14:20-14:35	Pain is a real issue in office gynaecological procedures <b>Gunvor Ekman-Ordeberg</b> , <i>Sweden</i>
14:35-14:50	What is the impact of oral contraceptives on sexual function in young women? <b>Angelica Lindén Hirschberg</b> , <i>Sweden</i>
14:50-15:05	Live chat Q&A

# ROLE OF OIL-SOLUBLE CONTRAST MEDIUM HYSTEROGRAPHY (OSCM-HSG) DURING THE FERTILITY WORK-UP

SATURDAY, NOVEMBER 21, 2020



14:05-15:05	HALL I
Chairperson	<b>Meenakshi Choudhary</b> , <i>UK</i>
14:05-14:20	Pregnancy and live birth outcomes after HSG with OSCM: How does the clinical evidence impact fertility management? <b>Velja Mijatovic</b> , <i>Netherlands</i>
14:20-14:35	OSCM-HSG: Safety profile <b>Emmeline Lee</b> , <i>Australia</i>
14:35-14:50	UK experience: Practical aspects and technical tips, fallopian tubes recanalization (FTR) <b>Elika Kashef</b> , <i>UK</i>
14:50-15:05	Q&A



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## INDUSTRY SESSION SPEAKER ABSTRACTS

# BioGaia®

### PROBIOTIC SUPPLEMENTATION DURING PREGNANCY

Flavia Indrio, Italy

Maternal microbiota represents the most important microbiota source for the neonatal microbiota colonization process. During the course of a normal pregnancy, several deep and dynamic physiological changes occur in the mother. Some of the endocrine and immune changes induced by pregnancy increase the susceptibility of the mother to various infections, including those of the oral cavity. During pregnancy, there is a reduction of antimicrobial activity of peripheral neutrophils, essential components of the innate immune defences of the periodontal tissues. This could be related to the well documented increase in gingival inflammation observed during pregnancy. One of the main changes in the immune system during pregnancy is the partial mitigation of the immune responses that are mediated by the mother's cells, as 50% of the antigens in the cells of the fetus are derived from the father, and these cells are chronically exposed to the mother's immune system. Several complex physiological changes are therefore induced during pregnancy in order to prevent immune rejection in the mother's body of her fetus. Increasing evidence suggests that maternal diet during pregnancy shapes the offspring's microbiota composition and intestinal development in the short and long term. During pregnancy, the female body adapts its metabolism, hormonal cascades and immunological events to optimize the growth of the foetus and prepare the body for lactation leading to similar markers to those observed in metabolic syndrome. Gut microbiota is also modified by changes, which have several consequences including increasing the energy extraction efficiency from the diet. Most studies of microbiota and dietary patterns have evaluated extreme diets (e.g., Western diet vs. non-Western diet) or diseased individuals (e.g., obese). However, the impact of diet and intestinal permeability during pregnancy on female microbiota and the possible subsequent health consequences are still not fully understood, specifically in healthy cohorts (non-obese) following a healthy standard diet. Few publications have shown that maternal diet can modulate the gut microbiome of the mother or infant. Thus, more information is required to address how nutrient patterns influence maternal and neonate gut microbiota. The role of probiotic supplementation and the role of these in changing the pattern of maternal microbiota will be discussed.



GEDEON RICHTER

### NEW APPROACHES TO OPTIMIZE ART OUTCOMES

#### RECEPTIVITY WINDOW EVALUATION TO IMPROVES ART OUTCOMES

Samir Hamamah

Department of ART/PGD, INSERM U 1203, Arnaud de Villeneuve hospital; Montpellier-34295, France

The evaluation of endometrial receptivity is crucial in Assisted Reproduction Technology (ART) programmes. Using our human transcriptomic data, we previously identified genes that are specifically over expressed in the endometrium during the implantation window and that could be potential biomarkers of endometrial receptivity. By using the molecular signature of these genes, we developed a diagnostic tool called Win-Test to evaluate the expression level of 11 specific biomarkers of endometrial receptivity during the implantation. Currently, there are only few tests to determine the endometrial receptivity status and to indicate the best timing for frozen embryo transfer (FET) during natural or hormone-supplemented cycles. However, these approaches are invasive and require an endometrial biopsy during the implantation window. Today, one of the ART challenges is the development of non-invasive tests in relation to the endometrial receptivity and the implantation window. MicroRNAs (miRNAs) are small non-coding RNA transcripts that regulate cell function by modulating the post-transcriptional activity of multiple target genes through repression of mRNA translation or regulation of mRNA degradation. The clinical benefits of miRNAs as diagnostic/prognostic biomarkers in blood and as therapeutic targets have been demonstrated in several diseases, including life-threatening pathologies. Many studies have provided evidence that miRNAs are crucial for cellular processes that occur during the cyclic endometrium changes. Moreover, aberrant miRNA expression has been associated with human endometrial disorders, such as endometriosis and carcinoma, and also with unexplained recurrent spontaneous miscarriage. In addition, certain miRNAs are circulating in blood and can be quantified in serum and plasma. The identification of endometrial receptivity-associated miRNAs in both endometrial biopsies and blood samples could open new perspectives for the development of a non-invasive endometrial receptivity test. In contrast to several recent studies that analysed the miRNome of endometrium samples during the different phases of the cycle or according to ART, here, we performed a miRNomic study to identify miRNAs during the implantation window that are associated with the receptivity status, and then according to the pregnancy outcome (implantation failure, early embryo miscarriage, and live birth at term) after customized FET. In addition, we tested some of the expressed miRNAs in serum samples.

## LUTEAL PHASE SUPPORT IN ART: INDIVIDUALIZATION OF PROGESTERONE TREATMENT

Elena Labarta, Spain

Luteal phase management during assisted reproduction is increasingly pursued for its potential to contribute to positive reproductive outcomes. Recent publications indicate that serum progesterone (P) levels in the mid luteal phase are associated with pregnancy outcome after embryo transfer in artificial cycles when using vaginal micronized progesterone. In fact, patients who exhibit low serum P levels show a significantly lower ongoing pregnancy rate and higher miscarriage rate. These findings suggest that a minimum level of serum P is required to optimize clinical outcome. Notably, these results can be extrapolated only to artificial cycles and, most importantly, use of vaginal natural-like progesterone, as preferred by many clinicians worldwide. Indeed, the pharmacokinetics and pharmacodynamics of vaginally-administered P differ from that of the intramuscular, subcutaneous or oral administration routes. For this reason, studies examining the role of serum P on pregnancy outcome cannot be compared when using different routes of administration. An international survey conducted some years ago, concluded that vaginal delivery is the preferred route of P administration in Europe. Vaginal delivery of P leads to higher uterine P levels due to the first uterine pass effect and lower serum P levels when compared with parenteral administration. The need to measure serum P is now apparent, but many questions remain. More research is needed to establish which is the best dose for each patient, according to the type of cycle, route of administration and individual characteristics. According to our results, one out of three patients receiving vaginal P showed inadequate levels of serum P, and this led to an 18% lower ongoing pregnancy rate. It is time to measure serum P levels and adapt the dose or the route according to the needs of the patient. Our experience reflects that this adjustment proves effective. Regarding the management of LPS in natural or stimulated cycles, the use of serum P as a biomarker is still being studied. One difficulty relies on the fact that in these cycles, there is a higher daily variation on serum P levels according to the pulsatile production of P by the corpus luteum, being one single determination insufficient to draw conclusions. In any case, the need for exogenous P in stimulated cycles is undoubtful, although in natural cycles this needs to be further studied. All these issues will be presented in detail in the lecture.

## PATIENT-ORIENTED COUNSELLING: PREDICTING LIVE BIRTH PROBABILITY (LBP) AT EACH STEP OF THE IN VITRO FERTILIZATION (IVF) PROCESS VIA MACHINE LEARNING.

Veronika Grzegorzczuk Martin, Spain

T. Fréour, C. Avril, A. de Bantel - Finet, P. Barrière, J.L.

Pouly, M. Grynberg, I. Parneix, J. Roset, T. M. Grzegorzczuk

**Introduction:** Many factors are known to have an impact on the chances of live birth when undergoing IVF treatment. Predictive models capable of predicting chances of success exist today and can greatly contribute to patient counselling and physician decision-making. To our knowledge, no model exists that dynamically adjusts the LBP throughout the IVF process, as new data become available. Our question was: How does a machine learning tool for live birth prediction accuracy evolve as demographic, ovarian stimulation, laboratory and transfer data become available? **Materials and Methods:** Data from 13574 fresh IVF cycles and 6770 subsequent frozen embryo transfers (2014-2017) in 5 IVF centres were retrospectively analysed. 48 Parameters were

included and split into four categories following the IVF process: (1) demographic (after the first consultation), (2) ovarian stimulation (during the stimulation), (3) laboratory (after the oocyte retrieval) and (4) transfer data (at the embryo transfer). These four categories were used to develop 4 predictive models. Only cycles with verified, consistent and complete data were included. We implemented a univariate and multivariate evolutive logistic regression, with iterative parameter selection based on 5% significance level. Validation was internally based on a 70%-30% split. Results are reported as odd ratios and C-index. LBP were recalculated at each step of the IVF process by fitting a new model at the addition of each of the four categories, finally yielding probabilities for each fresh or frozen embryo transfer.

**Results:** Accuracy of the model in predicting live birth progressively increased from 0.64 to 0.72 (C-index) as ovarian stimulation, laboratory and embryo transfer parameters were respectively added. Certain parameters were predictive in the all 4 models while other were predictive only in the 1<sup>st</sup> model and no longer in the subsequent when including new parameters. Female age remains strongly predictive of LBP at all steps. After fresh embryo transfers, LBP decreases linearly with increasing female age, whereas its impact becomes significant beyond 37 years for frozen transfers (OR=0.59; 95%CI=0.4-0.85). Female BMI influence is constant throughout all steps (OR=0.98; 95%CI=0.97-0.99). AFC and AMH are significant predictors when only baseline characteristics are included in the model, but their impact is not statistically significant anymore when the number of retrieved oocytes becomes available. High gonadotrophin dose negatively impacts LBP in fresh embryo transfers (OR=0.52; CI=0.42-0.64). Endometrial thickness positively impacts LBP at the transfer step (OR=1.07; CI=1.04-1.10).

**Conclusion:** This evolutive predictive model shows that the weight of individual parameters is not static but evolves at each step of IVF process, contributing to higher accuracies in live birth prediction (C-index). The prospect of this work is to develop an evolutive predictive tool capable of integrating new parameters throughout the IVF process, thus helping clinicians in patients counselling and decision making.



## GEDEON RICHTER

## UNSOLVED PROBLEMS IN WOMEN'S REPRODUCTIVE HEALTH

Supported by Gedeon Richter - Hungary

## DIAGNOSTIC AND THERAPEUTIC CHALLENGES OF RECURRENT VULVOVAGINAL CANDIDA INFECTIONS

Gilbert G.G. Donders

Femicare, Clinical Research for Women, Tienen, Belgium | University of Antwerp, Belgium

Complaints of possible vulvovaginitis, such as increased discharge, redness, pain, burning, itching or bad odor require a substantial diagnostic workout, that highly benefits from expertise and experience. Office microscopy is the cornerstone of an adequate management of vulvovaginitis, preventing unnecessary, time consuming and expensive lab testing. For Candida diagnosis in patients with recurrent VV

complaints, however, lab cultures, taken from patients at consultation or self sampled at home, can be a very useful additional tool. In the future, molecular nucleic acid amplification tests (NAAT) will be important for low grade and atypical yeast infections that can be difficult to visualize or harvest by culture. Another challenge is the understanding of the influence of the vaginal microbiome on the development or inhibition of yeast. Mixed infections occur in up to 30% of cases and pose a major therapeutic dilemma. As a consequence, the study probiotic influence of endogenous or exogenous lactobacilli and other bacteria is becoming a difficult, but promising challenge of modern research. Patients with recurrent yeast have to be followed properly and with care. Patients should be regarded as suffering from a chronic condition and treated in a similar fashion. We favor the ReCiDiF regimen for this purpose as it ensures a proper prophylactic treatment with a proper antifungal drug, combined with an adequate and well defined follow-up, while at the same protecting patients from overtreatment. Still, even despite such rigid regimens, some patients fail to get cured. Patient characteristics, such as genetic variations, underlying metabolic differences, or multiple site infections can influence the chances on cure, but also micro-organism derived factors play an important role. Amongst these, a shift towards azole resistant non-albicans types is the most important, as well as the growing evidence of increasing resistance of *Candida albicans* against most azoles. These issues pose major challenges for clinicians taking care of these hopeless patients who already suffer a great burden. In the absence of a vaccine in the near future, more intensive research on drugs that reinforce the activity of existing antifungals, combination of drugs with different modes of action and the introduction of new, potent drugs, with activity against a wide variety of candidal strains, are urgently needed. A brief update on all these items is given.

## PAIN - A REAL ISSUE IN OFFICE GYNAECOLOGICAL PROCEDURES

Gunvor Ekman-Ordeberg, MD, PhD  
Karolinska Institute, Sweden

**Problem statement:** Women undergoing office minor gynaecological procedures, experience significant pain. Currently there is no scientific consensus on the use of prophylactic pain treatment during these interventions. Even though pain is the primary reason for abandonment of procedure or incomplete assessment. Our aim was to present data on sensory innervation which complies to the pain perception in different minor gynaecological procedures.

**Methods:** Literature search was conducted using Embase and PubMed with a search string that incorporated the six most common minor gynaecological procedures (hysteroscopy-diagnostic or surgical, insertion of IUD, endometrial and vaginal biopsy, endometrial ablation, colposcopy of the cervix, conisation) in the office setting and focusing on pain experience. Time and language filters were applied, and results were collected from 2015 up to 29 July 2020 in English, which resulted in 34 hits. From this set of results, we identified the ones focusing on different attributes of pain, such as parity, anatomical conditions, neuroanatomical structures and technical background.

**Results:** Pain is a real issue in minor gynaecological procedures, which has a proven neuroanatomical background and multiple determinants. These include age and parity and circumstances, where pain experience might be even higher. Nulliparous young women tend to report higher pain scores. Technical premises, such as uterine filling pressure and instrument size may also influence the pain experience. Nevertheless, previous studies, carried out at Karolinska

Institute, showed that nociceptive nerve fibres were scattered throughout the uterus close to the mucosal layer. These findings explain the pain experience of women during office procedures. Additionally, it provides scientific basis for the use of local anaesthetics. This hypothesis is supported by the fact that benefits of the utilization of appropriate local anaesthetic outweigh the risks. **Conclusion:** There is an unmet need in minor office gynaecological procedures in terms of pain perception. Despite scientific foundation, there is no adequate local pain management. More gynaecological procedures could be performed in the office setting with appropriate local pain management. This should be the subject of further investigations.

## WHAT IS THE IMPACT OF ORAL CONTRACEPTIVES ON SEXUAL FUNCTION IN YOUNG WOMEN?

Angelica Lindén Hirschberg

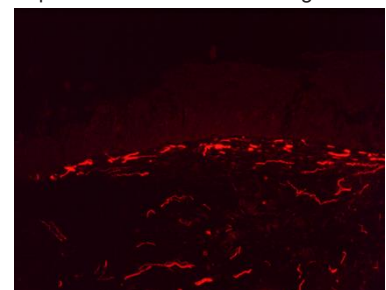
Department of Women's and Children's Health, Karolinska Institutet and Department of Gynecology and Reproductive Medicine, Karolinska University Hospital, Stockholm, Sweden

The oral contraceptive pill (OC) has been on the market for more than fifty years and has had a tremendous impact on women's reproductive health. Still, there is a lack of basic knowledge about how OC use may affect women's quality of life and sexuality. According to a systematic review based on observational studies, most OC users showed no significant change in libido, whereas 15% reported a decreased libido. In clinical practice, sexual dissatisfaction has been reported to be among the best predictors of OC discontinuation. Consequently, there may be a risk of unintended pregnancies and induced abortions due to reduced sexual desire.

Recently, two larger randomized placebo-controlled trials (RCTs) investigated the impact of OCs on sexual function in young healthy women. In our investigator-initiated study, we compared a first choice OC containing 150 µg levonorgestrel and 30 µg ethinylestradiol with placebo on sexuality in 340 young women. Using the validated instrument Profile of Female Sexual Function (PFSF), we found no overall effect on sexual function, whereas specific domains including desire, arousal and pleasure were significantly reduced in comparison to placebo. Another RCT, investigated an OC containing 1.5 mg estradiol and 2.5 mg norgestrel acetate and found a small decrease in sexual interest by the McCoy Female Sexuality Questionnaire compared to placebo. However, the clinical significance of these findings from the RCTs are not clear and have been debated. The mechanism by which OCs might affect libido is not elucidated. It has been suggested that an increase in sex hormone-binding globulin and thereby a decrease in free, biologically active testosterone could be a potential mechanism although there is no clear

relationship between levels of free testosterone and sexual desire. In this context the development of new OCs with the addition of the adrenal androgen,

dehydroepiandrosterone (DHEA) is of great interest.



## ROLE OF OIL-SOLUBLE CONTRAST MEDIUM HYSTEROSALPINGOGRAPHY (OSCM-HSG) DURING THE FERTILITY WORK-UP

**UK EXPERIENCE: PRACTICAL ASPECTS & TECHNICAL TIPS, FALLOPIAN TUBES RECANALIZATION (FTR)**  
**Elika Kashaf, London, UK**

Hysterosalpingography (HSG) is a commonly performed procedure however more recently it has become recognised that HSG's cannot be simply put onto a general fluoroscopy list. Building a patient rapport, taking a brief history, written consent and a dedicated HSG list performed by a trained specialist are setting the standard of practice for these cohort of patients. In this talk, the practical aspects of HSG will be covered along with some technical tips in challenging cases. Lipiodol HSG's are making an exciting comeback with promising results in increasing the likelihood of spontaneous pregnancy. The learning curve in Lipiodol HSG is quite steep and quite different to the standard HSG. Tips & tricks of a successful Lipiodol HSG will be covered in this lecture. Combining the skillsets of HSG and interventional radiology, fallopian tube recanalization can also be performed as part of the "Fertility treatment" in women. The talk will briefly demonstrate the technical aspects of FTRs.

### OIL-SOLUBLE CONTRAST MEDIUM – SAFETY ASPECTS **Dr. Emmeline Lee, Australia**

Oil-soluble contrast medium (OSCM), commonly known by its brand name Lipiodol® Ultra Fluid, was the original contrast medium used in hysterosalpingograms (HSG's). After falling out of fashion in the 1970's and 1980's, with the perceived extra safety of water-soluble contrast media (WSCM), Lipiodol® Ultra Fluid is now increasingly being used to increase the chance of pregnancy. Complications following Lipiodol® Ultra Fluid administration is reassuringly rare<sup>1</sup>. Though not common, it is important to recognize that they do occur, and when they do so, how to deal with them. Allergies, particular those that escalate to anaphylaxis is the most feared complication, especially by practitioners that work in an environment in which there is little medical support. Reassuringly, they do seem rather rare, and in a recent publication in which over 5000 had HSG's performed, none had documented anaphylaxis, and allergy in only 0.03% of patients, with no significant difference between OSCM and WSCM.<sup>1</sup> Radiation dose is another concern in the administration of any type of contrast in HSG's. This is due to the exposed area being the pelvis which contains gonads, and also, the fact that HSG's are performed in young women. Whether oil-or water-soluble, with modern techniques and equipment, radiation dose is not a lot, and averages approximately 5 mSv. Infections and pelvic inflammatory diseases are not common, with reported incidences of 0.3% in a few publications<sup>1</sup>. Granuloma formation is even less common, with only anecdotal evidence for this. Intravasation has become a potential issue, as there is a theoretical risk of oil embolism – pulmonary and cerebral. Tubal flushing with OSCM probably increased in the odds of intravasation (asymptomatic) compared to tubal flushing with WSCM (OR 5.00, 95% CI 2.25 to 11.12, 4 RCTs, 1912 women, 12 = 0,

moderate-quality evidence). This suggests that if the chance of intravasation following tubal flushing with WSCM is assumed to be 1%, the chance following tubal flushing with OSCM would be between 2% and 9%.<sup>2</sup> Embolism is rare, and though it has been reported<sup>3</sup>, was seen in a case where oil-soluble contrast was instilled without imaging guidance. Persistence of Lipiodol® can occur in the pelvis, and therefore potentially resulting in subclinical hypothyroidism. It has been reported that up to 25% of women develop subclinical hypothyroidism following oil-soluble contrast medium administration.<sup>4</sup> Reassuringly, our data shows slightly less incidence of this, though our group strongly advocates routine testing of thyroid function tests both before and after the administration of oil-soluble contrast medium. Thyroid function in neonates conceived after hysterosalpingography with iodinated contrast has also been questioned, but recent evidence has been reassuring, with no neonate conceived following HSG being affected by hypothyroidism.<sup>5</sup> Thus, it seems like complications are uncommon following oil-soluble contrast medium administration, which should bring comfort to both referrers and patients.

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### PREGNANCY & LIVE BIRTH OUTCOMES AFTER HSG WITH OIL SOLUBLE CONTRAST MEDIUM (OSCM): HOW DOES THE CLINICAL EVIDENCE IMPACT FERTILITY MANAGEMENT

**Velja Mijatovic, Consultant gynaecologist**  
 Department of Reproductive Medicine, Amsterdam UMC, Amsterdam, The Netherlands  
 On behalf of the H2Oil study group.

During fertility evaluation, HSG is one of the most commonly used tubal patency tests. HSG was initially introduced as a diagnostic test, however over the past decades it has emerged that it may influence the clinical outcomes, in terms of clinical pregnancy, over the patient journey. Recently, a systematic review and meta-analysis of six RCT's including the H2Oil trial was published [1]. This meta-analysis of 2,562 patients showed that the use of oil-soluble contrast media (OSCM) at HSG was associated with significantly higher ongoing pregnancy rates when compared to the use of water-soluble contrast (WSCM) corresponding with an OR of 1.47 (95% CI 1.12-1.93) in favor of OSCM. Although three trials reported on live birth in this meta-analysis, they were not pooled due to extreme statistical heterogeneity. In addition, a network meta-analysis on the fertility enhancing effects of tubal flushing with various contrast media confirmed these results [2]. This network meta-analysis showed that tubal flushing with OSCM led to more clinical pregnancies within six months, compared to tubal flushing with WSCM (OR 1.67, (95% CI 1.38-2.03; moderate quality of evidence) and no HSG

examination (OR 2.28, 95% CI 1.50-3.47; moderate quality of evidence). Both systematic reviews [1,2] show no difference in incidence of miscarriage or ectopic pregnancy between OSCM and WSCM groups confirming the findings of the H2Oil trial [3]. Recently, the long-term fertility and pregnancy outcomes of the H2Oil trial were published [4]. This study showed a significantly higher ongoing pregnancy rate in favor of HSG with the use of OSCM compared to WSCM within 5 years after randomization (80.0% in the OSCM group versus 75.0% in the WSCM group). Although this study showed a shorter time to ongoing pregnancy in favor of the use of OSCM, with a difference of almost four months, the absolute difference in ongoing pregnancies seen at six months did not increase over time. When analyzing only patients with pregnancies established via their Fallopian tubes, thus excluding IVF/ICSI pregnancies, the absolute difference in ongoing pregnancies (63.8% in the OSCM group versus 55.5% in the WSCM group) was higher than the absolute difference including the IVF/ICSI pregnancies. This points to a possible better effect with OSCM, as pregnancies established by IVF or ICSI are by-passing the Fallopian tubes. Furthermore, the curves representing the time to ongoing pregnancy within five years follow-up seem to be parallel, this possibly indicates a positive impact on clinical outcome by OSCM in the first months following HSG procedure. From the Dutch perspective, and based on the market prices of the year 2018, this results for OSCM in €2,327 mean costs for an ongoing pregnancy per couple and for WSCM in €2,471 [5]. With five years of follow-up, HSG using OSCM results in comparable costs (-€144; 95% CI -€579 – +€290,  $p=0.515$ ) for a 5% higher cumulative ongoing pregnancy rate compared with HSG using WSCM, making it the preferred strategy for tubal flushing.

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