



The 26th World Congress on
Controversies in Obstetrics,
Gynecology & Infertility (COGI)
All About Women's Health



In partnership with Reproductive BioMedicine Online (RBMO)

November 23-25, 2018
London, UK

Congress Program

COGI

Celebrating
40
years
of IVF

Timetable

Friday, November 23, 2018

	FLEMING	WHITTLE
14:30-15:30	THE BEST OF RBMO 2017-2018	
15:30-17:00	EPIGENETICS AND THE DOHaD CONCEPTS IN ART	LASER COURSE SMOOTH ERBIUM LASER FOR WOMEN'S HEALTH <i>see page 153</i>
17:00-18:30	FERTILITY PRESERVATION FOR SOCIAL MOTIVES	
18:30-19:30	OPENING SESSION NOBEL PRIZE LAUREATE ROBERT G. EDWARDS ANNUAL LECTURE BEST ABSTRACT AWARDS CEREMONY	
19:30-20:15	NETWORKING RECEPTION	

Saturday, November 24, 2018

	FLEMING	WHITTLE	ST. JAMES	WESTMINSTER	ABBEY
	INFERTILITY/ART/IVF	FETOMATERNAL MEDICINE	GYNECOLOGY	INFERTILITY/ART/IVF II	ORAL PRESENTATIONS
08:30-10:00	PCO/PCOS	ADVANCED MATERNAL AGE IN THE EYES OF THE EXPERTS; REPRODUCTIVE ENDOCRINOLOGISTS AND PERINATOLOGISTS	HRT: WHERE WE CAME FROM. WHERE ARE WE GOING?	SPECIAL COGI WORKSHOP: THE LWC SYMPOSIUM - BUILDING THE FUTURE FAMILY: HOW NEW TECHNOLOGIES ARE REDEFINING FAMILY PLANNING I	ORAL PRESENTATIONS 01 - ART/IVF/INFERTILITY
10:00-10:20	<i>Coffee break and poster viewing</i>				
10:20-11:50	USE, ABUSE AND UNDERUSE OF PROCEDURES	PROGESTERONE AND ESTROGENS: WHAT TO KNOW FOR ART A PREIS SCHOOL ACADEMY SESSION	HRT PRESCRIBING: MAKING THE SCIENCE APPLICABLE IN THE REAL WORLD	SPECIAL COGI WORKSHOP: THE LWC SYMPOSIUM - BUILDING THE FUTURE FAMILY: HOW NEW TECHNOLOGIES ARE REDEFINING FAMILY PLANNING II	ORAL PRESENTATIONS 02 - GYNECOLOGY
11:50-12:10	<i>Break</i>				
12:10-13:40	INDUSTRY SUPPORTED SESSION <i>see page 154</i>	SPECIAL WORKSHOP ON PREVENTION AND MANAGEMENT OF BLEEDING IN PREGNANCY: ALL ABOUT PPH PREVENTION	INDUSTRY SUPPORTED SESSION <i>see page 155</i>	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: ARE WE MAKING ADVANCES IN THE LABORATORY?	ORAL PRESENTATIONS 03 - FETOMATERNAL MEDICINE
13:40-14:30	<i>Lunch break and poster viewing</i>				
14:30-16:30	IMPLANTATION FAILURE AND WHAT'S NEXT	SPECIAL WORKSHOP ON PREVENTION AND MANAGEMENT OF BLEEDING IN PREGNANCY: TREATMENT	HRT AND BREAST CANCER	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: WHAT MAKES A GOOD EMBRYO?	ORAL PRESENTATIONS 04 - GYNECOLOGY
16:30-16:50	<i>Coffee break and poster viewing</i>				
16:50-18:20	CONTROL OVARIAN STIMULATION	MISCARRIAGE AND ART	PREMATURE OVARIAN INSUFFICIENCY- POI: ADVANCES IN DIAGNOSIS AND MANAGEMENT	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: EXTENDED SCREENING	ORAL PRESENTATIONS 05 - FETOMATERNAL MEDICINE

Sunday, November 25, 2018

	FLEMING	WHITTLE	ST. JAMES	WESTMINSTER	ABBEY
	INFERTILITY/ART/IVF	FETOMATERNAL MEDICINE	GYNECOLOGY	INFERTILITY/ART/IVF II	ORAL PRESENTATIONS
08:30-10:00	ENDOMETRIOSIS ADENOMYOSIS	PRENATAL DIAGNOSIS AFTER ASSISTED REPRODUCTION	SLS: UPDATES ON THE STATE OF THE ART OF MINIMALLY INVASIVE SURGERY TO PRESERVE FERTILITY	MOSAICISM	ORAL PRESENTATIONS 01 - FETOMATERNAL MEDICINE
10:00-10:20	<i>Coffee break and poster viewing</i>				
10:20-11:50	ET AND LUTEAL SUPPORT	PREVENTION OF PREMATURE BIRTH	GENERATING AN HPV DIAGNOSIS IN A SCREENING EVENT	JOINT COGI-ISMAAR SESSION	ORAL PRESENTATIONS 02 - ART/IVF/INFERTILITY
11:50-12:10	<i>Break</i>				
12:10-13:40	GENETIC TESTING OF EMBRYOS	PREDICTION, PREVENTION MANAGEMENT OF PRECLAMPسيا	HPV VACCINES: LIGHTS AND SHADOWS	SPECIAL WORKSHOP HISTORY OF IVF: PART I	ORAL PRESENTATIONS 03 - ART/IVF/INFERTILITY
13:40-14:30	<i>Lunch break and poster viewing</i>				
14:30-16:30	IVF: LESS IS MORE?	HOT CONTROVERSIES	PREMATURE OVARIAN FAILURE	SPECIAL WORKSHOP HISTORY OF IVF: PART II	ORAL PRESENTATIONS 04 - FETOMATERNAL MEDICINE
16:30-16:50	<i>Coffee break and poster viewing</i>				
16:50-18:20	RTD ON PROVEN AND UNPROVEN ART PROCEDURES	GESTATIONAL DIABETES AND OBESITY	MENOPAUSE AND PERIMENOPAUSE		ORAL PRESENTATIONS 05 - GYNECOLOGY

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ELSEVIER



Bart Fauser
Chief Editor

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and on Twitter [@RBMOnline](https://twitter.com/RBMOnline)

Words of Welcome from COGI Chairpersons

Dear Friends and Colleagues,

Welcome to the 26th World Congress on Controversies in Obstetrics, Gynecology and Infertility (COGI) and RBMOnline, celebrating 40 years of IVF in the magnificent city of London.

World renowned leaders in the field, both past and present, will review advances and breakthroughs via stories, history, debates, controversies and round table discussions. There will be critical reviews of where we came from and predictions for where we are heading. Highlights will include the “Robert G Edwards Nobel Prize Laureate” lecture, newly conceived “countercurrent” lectures by leading experts, as well as an inspiring fetomaternal medicine program and its relationship to IVF, sessions on early prenatal diagnosis, pregnancy support, age-related risks, nutrition, the epidemic of multiple pregnancies, gynecological infertility-related diseases, and more. As always, there will be ample time in every session for speaker-audience discussions.

We would like to thank the industry for their ongoing support of the COGI Congresses. Without this support, we would not be able to host a congress where education and knowledge is shared on such a high level.

We welcome all our delegates from around the globe who have travelled to join us at this unique congress and we look forward to enjoyable discussions, thought-provoking debates and an overall excellent congress experience.

We invite you to join us again in 2019, in Paris, France where the COGI experience will continue.

Sincerely,

Congress Chairpersons



Zion Ben Rafael
Israel



Bart C.J.M. Fauser
The Netherlands



Simon Fishel
UK



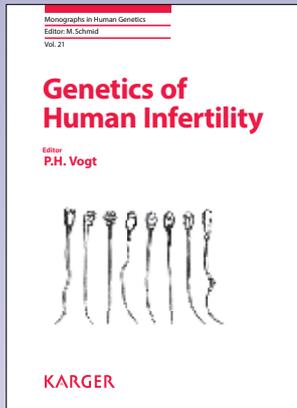
Rene Frydman
France



Nick Panay
UK



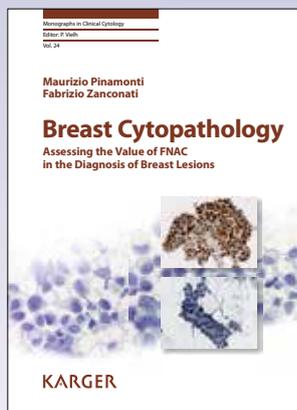
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Monographs in Human Genetics, Vol. 21
Genetics of Human Infertility

Editor: **Vogt, P.H.** (Heidelberg)
X + 178 p., 24 fig., 16 in color, 8 tab., 2017
ISBN 978-3-318-06097-3

www.karger.com/mhg



Monographs in Clinical Cytology, Vol. 24
Pinamonti, M.; Zancanati, F. (Trieste)

Breast Cytopathology
Assessing the Value of FNAC in
the Diagnosis of Breast Lesions

VI + 118 p., 126 fig., 119 in color,
hard cover, 2018
ISBN 978-3-318-06140-6

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General Information

VENUE

QEII Centre London
Broad Sanctuary
Westminster
London, SW1P 3EE

LANGUAGE

The official language of the congress is English.

REGISTRATION AND FACULTY DESK OPENING HOURS

Friday, November 23	12:30-20:00
Saturday, November 24	07:30-18:30
Sunday, November 25	08:00-18:30

CONGRESS ADMISSION – NAME BADGE

Admission to the scientific sessions, exhibition area and congress-related events is by badge only. All participants are kindly requested to carry their personal badge received upon registration at all times while at the congress.

EXHIBITION OPENING HOURS

Friday, November 23	19:00-20:15
Saturday, November 24	09:30-17:00
Sunday, November 25	09:30-17:00

POSTERS

All the posters are presented in electronic format. The stations are located on the third floor and will be open to all participants on Friday, Saturday and Sunday during the exhibition hours.

INTERNET

Wi-Fi is available to all congress delegates.

Username: **cogi**

Password: **london2018**

CERTIFICATE OF ATTENDANCE (non-CME/CPD)

You may collect your certificate of attendance from the registration desk. The certificates will be handed out from Sunday, November 25.

CME ACCREDITATION

The 26th COGI Congress has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) for a maximum of 20 European CME credits (ECMEC®s).

To receive your CME accreditation certificate, please visit the congress website and complete the online form. Your certificate will be sent to you directly following the congress.

REFRESHMENTS

The networking reception will be held on Friday, November 23 at 19:30 in the exhibition area on the third floor (Britten Suite).

Coffee and lunch will be served in the exhibition area on Saturday, 24 and Sunday, 25 November during the official catering breaks.

SPEAKERS' PREVIEW ROOM

All invited speakers and oral presenters are asked to upload their presentations at the speakers' preview room (Brunel Room - Ground floor, next to the registration area) at least 2 hours before the start of their session. The room will be open during the following hours:

Friday, November 23	12:30-19:00
Saturday, November 24	07:30-18:00
Sunday, November 25	08:00-18:00



CLOAKROOM

The cloakroom is located on the ground floor and will be open during the following hours:

Friday, November 23	14:00-20:00
Saturday, November 24	07:30-18:30
Sunday, November 25	08:00-18:30

SAFETY AND SECURITY

Please do not leave any bags or other personal belongings unattended at any time, whether inside or outside the session halls.

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 26th COGI Congress. Participants are advised to make their own arrangements with respect to health and travel insurance.

RECORDING POLICY

Recording (photographic, video and audio) of the session is strictly prohibited.

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**

COGI AT YOUR FINGERTIPS

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COGI is proud to introduce the Congress APPLICATION – a state-of-the-art educational tool dedicated to implementing innovative and environmentally-friendly technology.

The COGI App is your best tool for planning and organizing your participation and keeping up to date.

The App can be downloaded via your personal device through both Google Play and Apple stores. In

order to access the COGI congress program, abstracts and other information, please scan the relevant QR code or click on the relevant short link below:

All Devices

(with this you are able to choose between android or ios once you click on the link or scan the QR code)

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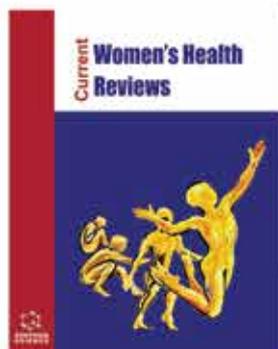


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JOURNALS FROM BENTHAM SCIENCE

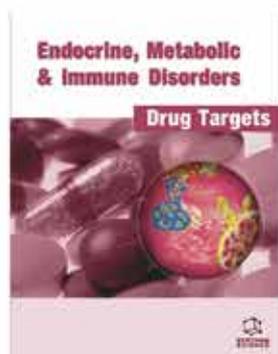


Current Women's Health Reviews

Volume 14, 3 Issues, 2018
ISSN: 1573-4048 (Print)

Current Women's Health Reviews publishes original research papers, frontier reviews, drug clinical trial studies and guest edited thematic issues written by leaders in the field covering a range of current topics on obstetrics and gynecology. The journal's aim is to publish the highest quality articles dedicated to research in the field. The journal is essential reading for all clinicians and researchers in the fields of obstetrics and gynecology.

Editor-in-Chief:
John Yeh
USA

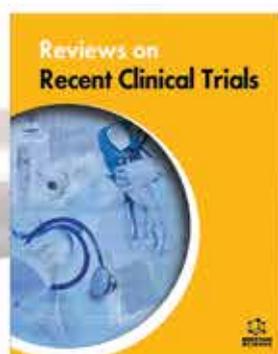


Endocrine, Metabolic & Immune Disorders - Drug Targets

Volume 18, 6 Issues, 2018
ISSN: 1871-5303 (Print)

This journal is devoted to timely reviews and original articles of experimental and clinical studies in the field of endocrine, metabolic, and immune disorders. Specific emphasis is placed on humoral and cellular targets for natural, synthetic, and genetically engineered drugs that enhance or impair endocrine, metabolic, and immune parameters and functions. Moreover, the topics related to effects of food components and/or nutraceuticals on the endocrine-metabolic-immune axis and on microbiota composition are welcome.

Editor-in-Chief:
Emilio Jirillo
Italy



Reviews on Recent Clinical Trials

Volume 13, 4 Issues, 2018
ISSN: 1574-8871 (Print)

Reviews on Recent Clinical Trials publishes high quality frontier reviews, original research articles, interesting case reports, drug clinical trial studies and guest edited thematic issues on recent clinical trials of major importance. The journal's aim is to publish the highest quality articles in the field. Topics covered include: important Phase I – IV clinical trial studies, clinical investigations at all stages of development, therapeutics, meta analysis, trial logistics, design and conduct of trials, statistical methods, synthesis and evidence evaluation, decision analysis, reviews, case reports and commentaries on current or controversial issues.

Editor-in-Chief:
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Italy

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COGI

All About Women's Health

Scientific Program



FRIDAY, NOVEMBER 23, 2018

JOINT SESSIONS: FMM /ART/IVF

14:30-15:30	THE BEST OF RBMO 2017-2018	FLEMING
Capsule	The editor's selection of the best publications	
Chairperson	Bart Fauser , <i>Netherlands</i>	
14:30-14:50	Increased miscarriage of euploid pregnancies in obese women undergoing cryopreserved embryo transfer Kelton Tremellen , <i>Australia</i>	
14:50-15:10	Increased insulin resistance in men with unexplained infertility Ragaa Mansour , <i>Egypt</i>	
15:10-15:30	Ovarian tissue cryopreservation in female-to-male transgender people: Insights into ovarian histology and physiology after prolonged androgen treatment Chloë De Roo , <i>Belgium</i>	

15:30-17:00	EPIGENETICS AND THE DOHaD CONCEPTS IN ART <i>FMM and ART session</i>	FLEMING
Capsule	Perinatal maternal conduct and conditions have profound effects on the long-term health of a newborn. What do we know? What do we think we know? What the reproductive and FMM specialists should know. This is a combined ART and FMM session with leaders in the field discussing the DOHaD concept from different perspectives.	
Chairpersons	Lucilla Poston , <i>UK</i> Nick Macklon , <i>UK</i>	
15:30-15:55	The DOHaD concept and long-term effects Gian Carlo Di Renzo , <i>Italy</i>	
15:55-16:15	Epigenetics and ART Jordana Bell , <i>UK</i>	
16:15-16:40	Nutrition, ART and outcome Nick Macklon , <i>UK</i>	
16:40-17:00	Obesity, ART and outcome Lucilla Poston , <i>UK</i>	

17:00-18:30	FERTILITY PRESERVATION FOR SOCIAL MOTIVES	FLEMING
Capsule	Freezing for social motives is like buying insurance for future fertility, and is flourishing as a new service, but is also a source of new income for IVF clinics from patients of untested fertility. The new field of ovarian tissue freezing has expanded the possibilities of postponing menopause and fertility. However, authentic discussions on cost effectiveness for the society is missing.	
Chairpersons	Alan DeCherney , <i>USA</i> Laura Rienzi , <i>Italy</i>	
17:00-17:45	Debate: Social freezing: What are the results of oocyte survival, pregnancy rate and obstetrics outcome? The procedure is very effective and can ensure future fertility: Ana Cobo , <i>Spain</i> Results of freezing are not as good as published: Norbert Gleicher , <i>USA</i>	
17:45-18:05	Can we use ovarian tissue cryopreservation to delay menopause? More mothers after 50? Jacques Donnez , <i>Belgium</i>	
18:05-18:30	Freezing for social motives is not cost effective for society! Zion Ben Rafael , <i>Israel</i>	



18:30-19:30	OPENING SESSION	FLEMING
Capsule	What have we learned from 40 years of the ever-evolving IVF experience? Writing the history pages of the IVF book.	
Chairpersons	Zion Ben Rafael , <i>Israel</i> Bart Fauser , <i>Netherlands</i> Rene Frydman , <i>France</i>	
18:30-19:15	Nobel Prize Laureate Robert G. Edwards annual lecture The long and winding road to success in ART/IVF Alan DeCherney , <i>USA</i>	
19:15-19:30	Best Abstract Awards Ceremony	

19:30-20:15	NETWORKING RECEPTION	EXHIBITION AREA
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15:30-18:30	LASER COURSE <i>see page 153</i>	WHITTLE
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SATURDAY, NOVEMBER 24, 2018

INFERTILITY/ART/IVF

08:30-10:00	PCO/PCOS	FLEMING
Capsule	The definition of PCO/PCOS has changed several times during the last 4 decades. Should we change it again? Despite our better understanding, the treatment remains a challenge.	
Chairpersons	Bart Fauser , <i>Netherlands</i> Phillippe Bouchard , <i>France</i>	
08:30-08:55	Defining the polycystic ovary: AMH or ultrasound? Antonio La Marca , <i>Italy</i>	
08:55-09:15	WHO consensus algorithm for management of anovulatory PCOS Phillippe Bouchard , <i>France</i>	
09:15-09:40	New insights into the PCOS Joop Laven , <i>Netherlands</i>	
09:40-10:00	Does Cochrane reviews show any role for metformin in the management of PCOS? Thomas Tang , <i>UK</i>	

10:00-10:20 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

10:20-11:50	USE, ABUSE AND UNDERUSE OF PROCEDURES	FLEMING
Capsule	IVF has seen many technologies that have come and gone, and were used and abused. What is the future of these technologies?	
Chairpersons	Joop Laven , <i>Netherlands</i> Nikolaos Polyzos , <i>Spain</i>	
10:20-10:45	ICSI: From the beginning to where we are today / Are we abusing ICSI? Gianpiero Palermo , <i>USA</i>	
10:45-11:05	The end of freeze all? Pasquale Patrizio , <i>USA</i>	
11:05-11:30	IVM: The rise and fall and rise again of IVM? Johan Smitz , <i>Belgium</i>	
11:30-11:50	Achieving deliveries in primary ovarian insufficiency Kazuhiro Kawamura , <i>Japan</i>	

11:50-12:10 BREAK

12:10-13:40	INDUSTRY SYMPOSIUM	FLEMING
	<i>see page 154</i>	

13:40-14:30 LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA



14:30-16:30	IMPLANTATION FAILURE AND WHAT'S NEXT	FLEMING
Capsule	After a few failures, physicians are expected to provide an explanation and modify the treatment. However no widely accepted definition repeated implantation failure (RIF) exist and so the reason remains mostly vague. Despite recent advances in our understanding, we do not have good solutions other than keep treating.	
Chairpersons	Frank Broekmans , <i>Netherlands</i> Dong Zi Yang , <i>China</i> Johan Smitz , <i>Belgium</i>	
14:30-14:55	The endometrium in repeated implantation failure Nick Macklon , <i>UK</i>	
14:55-15:15	High-throughput single-cell RNA-seq analysis of the endometrium associated with recurrent pregnancy loss Jan Brosens , <i>UK</i>	
15:15-15:40	Immunology and implantation Nathalie Ledee , <i>France</i>	
15:40-16:00	Does RIF exist? Edgardo Somigliana , <i>Italy</i>	
16:00-16:30	Special COGI countercurrent lecture: IVF outcomes over the years. Is LBR rising or declining? Why? Norbert Gleicher , <i>USA</i>	

16:30-16:50 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	CONTROL OVARIAN STIMULATION	FLEMING
Capsule	The first step in IVF is probably the most crucial and yet it varies so significantly in different centers as to prevent real comparisons. Many questions are still open despite years of studies. Why use more than 225 IU of FSH, and why not use hCG for luteal support? Should we report results of one-year outcome or keep it the usual way?	
Chairpersons	Norbert Gleicher , <i>USA</i> Canquan Zhou , <i>China</i> Rene Frydman , <i>France</i>	
16:50-17:15	Why do we think more eggs is better than less eggs? Is it in the quality only? Ben Mol , <i>Australia</i>	
17:15-17:35	Why still use FSH dosages over 225 IU? Frank Broekmans , <i>Netherlands</i>	
17:35-17:55	When hCG was the luteal support drug: Will it be the come-back kid? Claus Yding Andersen , <i>Denmark</i>	
17:55-18:20	Which outcome should be reported in IVF? Let's move to one-year outcome Bart Fauser , <i>Netherlands</i>	



SATURDAY, NOVEMBER 24, 2018

INFERTILITY/ART/IVF II

08:30-10:00	SPECIAL COGI WORKSHOP: THE LWC (LONDON WOMEN'S CLINIC) SYMPOSIUM - BUILDING THE FUTURE FAMILY: HOW NEW TECHNOLOGIES ARE REDEFINING FAMILY PLANNING I	WESTMINSTER
Chairperson	Nick Macklon, UK	
08:30-09:00	Finding a donor: Trust the clinic or do it yourself Joyce Harper, UK	
09:00-09:30	The rise of cross border egg donation Vanessa Vergara-Bravo, Italy	
09:30-10:00	Egg donation in UK: Regulations and technology influence patient behavior Kamal Ahuja, UK	

10:00-10:20 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

10:20-11:50	SPECIAL COGI WORKSHOP: THE LWC (LONDON WOMEN'S CLINIC) SYMPOSIUM - BUILDING THE FUTURE FAMILY: HOW NEW TECHNOLOGIES ARE REDEFINING FAMILY PLANNING II	WESTMINSTER
Chairperson	Bart Fauser, Netherlands	
10:20-10:45	Seeking perfection: Extended carrier screening in egg donation Amelia Rodriguez-Aranda, Spain	
10:45-11:05	Families created by identity-release egg donation Susan Golombok, UK	
11:05-11:30	The threats of technology to laws of disclosure: Is anonymity still realistic? Guido Pennings, Belgium	
11:30-11:50	Regulatory implications in the UK for cross border movement of frozen gametes Nick Jones, UK	

11:50-12:10 BREAK

12:10-13:40	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: ARE WE MAKING ADVANCES IN THE LABORATORY?	WESTMINSTER
Session	Laboratory work	
Capsule	Time lapse use is growing. What advantages does it provide? Can we improve embryo quality?	
Chairpersons	Cristina Hickman, UK Roger Sturmey, UK	
12:10-12:35	Time-Lapse: Useful algorithms or just nice videos? Alison Campbell, UK	
12:35-12:55	Can artificial intelligence help to select viable embryos? Cristina Hickman, UK	
12:55-13:20	What can be done to improve embryo culture? Laura Rienzi, Italy	
13:20-13:40	What biomarkers are worth measuring? Roger Sturmey, UK	



13:40-14:30**LUNCH BREAK AND POSTER VIEWING****EXHIBITION AREA**

14:30-16:30	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: WHAT MAKES A GOOD EMBRYO?	WESTMINSTER
Session	Improving embryo quality	
Capsule	Can we improve embryo quality or just select the good one?	
Chairpersons	Laura Rienzi , <i>Italy</i> Stephen Harbottle , <i>UK</i>	
14:30-15:00	Progress with in vitro maturation Evelyn Telfer , <i>UK</i>	
15:00-15:30	CRISPR editing of the human embryo Helen O'Neill , <i>UK</i>	
15:30-16:00	A design for life: How to get the most out of your laboratory Stephen Harbottle , <i>UK</i>	
16:00-16:30	Special COGI-RBMO countercurrent lecture: Aneuploidy and mosaic embryos can be transferred Siobhan Quenby , <i>UK</i>	

16:30-16:50**COFFEE BREAK AND POSTER VIEWING****EXHIBITION AREA**

16:50-18:20	SPECIAL COGI & ALPHA SOCIETY WORKSHOP SESSION: EXTENDED SCREENING	WESTMINSTER
Capsule	Global screening is increasingly used, but do we have evidence of its cost effectiveness? Why do we need to screen all donors?	
Chairpersons	Joyce Harper , <i>UK</i> Rita Vassena , <i>Spain</i>	
16:50-17:35	<u>Debate:</u> Global re-evaluation of genetic testing in-light of the most recent advancements Evidences are still lacking: Norbert Gleicher , <i>USA</i> Evidences have been achieved: Laura Rienzi , <i>Italy</i>	
17:35-18:00	Should we fully screen all donors or only if the male is a carrier? Rita Vassena , <i>Spain</i>	
18:00-18:20	An update on reproductive genetics. What does the future hold? Joyce Harper , <i>UK</i>	



SATURDAY, NOVEMBER 24, 2018

GYNECOLOGY

08:30-10:00	HRT: WHERE WE CAME FROM. WHERE ARE WE GOING?	ST. JAMES
Capsule	Despite the many years that have lapsed and the proof to the contrary, we are still dwelling under the shadows of WHI	
Chairpersons	Alesandra Graziottin , <i>Italy</i> Santiago Palacios , <i>Spain</i>	
08:30-08:50	Lights and shadows in WHI: A never ending nightmare! Mark Brincat , <i>Malta</i>	
08:50-09:10	HRT for primary prevention? John Stevenson , <i>UK</i>	
09:10-09:35	Selective estrogen receptor modulators Santiago Palacios , <i>Spain</i>	
09:35-10:00	Clinical data and national/international guidelines Nick Panay , <i>UK</i>	

10:00-10:20 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

10:20-11:50	HRT PRESCRIBING: MAKING THE SCIENCE APPLICABLE IN THE REAL WORLD	ST. JAMES
Capsule	The development of alternatives to HRT to treat vaginal atrophy was accelerated due to the sharp drop in HRT following WHI.	
Chairpersons	Santiago Palacios , <i>Spain</i> Mark Brincat , <i>Malta</i>	
10:20-10:45	HRT Treatment: Are they all the same Nick Panay , <i>UK</i>	
10:45-11:10	Practical approach to HRT treatment Louise Newson , <i>UK</i>	
11:10-11:50	<u>Debate:</u> Vaginal laser: Erbium or Co2 – which has superior data? Erbium: Marco Gambacciani , <i>Italy</i> Co2: Santiago Palacios , <i>Spain</i>	

11:50-12:10 BREAK

12:10-13:40	INDUSTRY SYMPOSIUM <i>see page 155</i>	ST. JAMES
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13:40-14:30 LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA



14:30-16:30	HRT AND BREAST CANCER	ST. JAMES
Capsule	Do we know if Estrogens are protective or carcinogenic for the breast?	
Chairpersons	Mark Brincat , <i>Malta</i> Pierluigi Benedetti Panici , <i>Italy</i>	
14:30-14:50	WHO claims, "Estrogens are carcinogenic". Is this true? Christian Singer , <i>Austria</i>	
14:50-15:15	Can HRT and treatment for menopause be individualized to reduce the incidence of breast cancer? Mark Brincat , <i>Malta</i>	
15:15-15:35	Results of high dose estetrol (E4) treatment in women with advanced breast cancer Arnd Höinig , <i>Germany</i>	
15:35-16:00	HRT in cancer survivors Pierluigi Benedetti Panici , <i>Italy</i>	
16:00-16:30	Special countercurrent lecture: Estrogens can protect against breast cancer Herjan Coelingh Bennink , <i>Netherlands</i>	

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	PREMATURE OVARIAN INSUFFICIENCY- POI: ADVANCES IN DIAGNOSIS AND MANAGEMENT	ST. JAMES
Capsule	Can better understanding help in providing treatment to this frustrating condition?	
Chairpersons	Nick Panay , <i>UK</i> Brianna Cloke , <i>UK</i>	
16:50-17:10	Does the type of HRT matter in POI? Monica Mittal , <i>UK</i>	
17:10-17:30	100,000 genomes project to unravel etiology of early POI Brianna Cloke , <i>UK</i>	
17:30-17:55	Global POI registry to optimize management Nick Panay , <i>UK</i>	
17:55-18:20	ESHRE POI guidelines: Where to next? Lisa Webber , <i>UK</i>	



SATURDAY, NOVEMBER 24, 2018

FETOMATERNAL MEDICINE

08:30-10:00	ADVANCED MATERNAL AGE IN THE EYES OF THE EXPERTS; REPRODUCTIVE ENDOCRINOLOGISTS AND PERINATOLOGISTS	WHITTLE
Capsule	What is considered advanced maternal age and what are the risks	
Chairpersons	Isaac Blickstein, Israel Stuart Lavery, UK	
08:30-08:55	The impact of advanced maternal age on maternal health: Long term effect Asma Khalil, UK	
08:55-09:15	From which maternal age should we apply special preconception tests: FMM Point of view Stuart Lavery, UK	
09:15-09:40	Advanced Maternal Age: Until what age autologous and until when homologous eggs? Reproductive endocrinologist's point of view Norbert Gleicher, USA	
09:40-10:00	When are you too old to shake the cradle? The impact of maternal age on pregnancy outcome Yariv Yogev, Israel	

10:00-10:20
COFFEE BREAK AND POSTER VIEWING
EXHIBITION AREA

10:20-11:50	PROGESTERONE AND ESTROGENS: WHAT TO KNOW FOR ART A PREIS SCHOOL ACADEMY SESSION	WHITTLE
Capsule	Progesterone, the main hormone during pregnancy, is commonly used to support normal and abnormal pregnancy from implantation to prevention of miscarriages to delaying labor.	
Chairpersons	Rene Frydman, France Roberto Palermo, Italy	
10:20-10:40	Pharmacodynamics of progesterone: What to know Paul Piette, Belgium	
10:40-11:00	Benefits and limits of sexual hormones Michael Schumacher, France	
11:00-11:25	Luteal phase support Rene Frydman, France	
11:25-11:50	Choice of protocols for pregnancy support Roberto Palermo, Italy	

11:50-12:10
BREAK

12:10-13:40	SPECIAL WORKSHOP ON PREVENTION AND MANAGEMENT OF BLEEDING IN PREGNANCY: ALL ABOUT PPH PREVENTION	WHITTLE
Capsule	Perinatal bleeding is a dramatic, life threatening emergency, necessitating preventive steps and a firm clinical and medical response. The objective is to identify and intervene early.	
Chairperson	Sabaratnam Arulkumaran, UK	
12:10-12:15	Introduction Sabaratnam Arulkumaran, UK	
12:15-12:40	Rethinking PPH prevention: CHAMPION study Metin Gulmezoglu, WHO-Switzerland	



12:40-13:05	Cochrane PPH prevention meta-analyses in 2018 Ioannis Gallos, UK
13:05-13:30	Rethinking PPH prevention: IMox study Helen Van der Nelson, UK
13:30-13:40	Close – Q&A Panel discussion

13:40-14:30

LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA

14:30-16:30	SPECIAL WORKSHOP ON PREVENTION AND MANAGEMENT OF BLEEDING IN PREGNANCY: TREATMENT	WHITTLE
Capsule	Perinatal bleeding is a dramatic, life threatening emergency, necessitating preventive steps and a firm clinical and medical response. The objective is to identify and intervene early.	
Chairpersons	Dan Farine, Canada Gian Carlo Di Renzo, Italy	
14:30-14:50	Team training in obstetrics Cressida Bond, UK	
14:50-15:10	Management of postpartum hemorrhage Edwin Chandharan, UK	
15:10-15:35	Etiology of PPH in twins Isaac Blickstein, Israel	
15:35-16:00	Tranexamic acid in the management of postpartum hemorrhage Sabataram Arulkumaran, UK	
16:00-16:30	Special countercurrent lecture: From RCTs to clinical guidelines - How could we go wrong? 3 examples where excellent RCT created problems Dan Farine, Canada	

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	MISCARRIAGE AND ART	WHITTLE
Capsule	How can we prevent pregnancy failure?	
Chairpersons	Yacoub Khalaf, UK Katerina Jeremic, Serbia	
16:50-17:10	Fibroids and repeated pregnancy failure Yacoub Khalaf, UK	
17:10-17:35	Uterine niche: When should we treat? Leila Adamyan, Russia	
17:35-17:55	Immunology of pregnancy: What should we know? Anke Diemert, Germany	
17:55-18:20	Special lecture: Should all women be induced at 39 weeks – The results of the ARRIVE trial Dan Farine, Canada	



SATURDAY, NOVEMBER 24, 2018

ORAL PRESENTATIONS

08:30-10:00	ORAL PRESENTATION 1 – INFERTILITY/ART/IVF	ABBEY
Chairpersons	Mattheos Fraidakis , <i>Greece</i> Aleksandar Stefanović , <i>Serbia</i>	
08:30-08:40	OP1-101 Intrauterine administration of human chorionic gonadotropin (hCG) for subfertile women undergoing assisted reproduction: a systematic review and meta-analysis Nikolaos Tsampras , <i>UK</i>	
08:40-08:50	OP1-102 The relationship between the elevated preovulatory and postovulatory progesterone serum concentration and the outcome of in vitro fertilization Emina Ejubovic , <i>Bosnia and Herzegovina</i>	
08:50-09:00	OP1-103 Role of progesterone level on day of hCG injection in IVF cycles on clinical pregnancy rate Ashmita Jawa , <i>India</i>	
09:00-09:10	OP1-104 The association between circulating Neuregulin 4 levels, metabolic, aetrogenic and AMH profile of polycystic ovary syndrome Meryem Kurek Eken , <i>Turkey</i>	
09:10-09:20	OP1-105 Impact of ethnicity on fresh and frozen embryo transfer outcomes Mariano Mascarenhas , <i>UK</i>	
09:30-09:40	OP1-106 MTHFR SNPs consequences on gametes and embryos affect equally men and women fertility and can be overcome with treatment: 5MTHF with one carbon cycle support (1-CC) Patrice Clement , <i>France</i>	

10:00-10:20
COFFEE BREAK AND POSTER VIEWING
EXHIBITION AREA

10:20-11:50	ORAL PRESENTATION 2 - GYNECOLOGY	ABBEY
Chairpersons	George Creatsas , <i>Greece</i> Bari Kaplan , <i>Israel</i>	
10:20-10:29	OP1-201 The role of antibodies to steroid hormones and chemical carcinogen benzo[a]pyrene in women with endometriosis Natalia Artymuk , <i>Russia</i>	
10:29-10:38	OP1-202 Adenomyosis: Role of stem cells markers in the pathogenesis Irena Kozachenko , <i>Russia</i>	
10:38-10:47	OP1-203 Ectopic pregnancies in unusual locations Silvaine Dalli , <i>Malta</i>	



10:47-10:56	OP1-204 How vaginal microbiota's re-establishment can reduce sexually transmitted diseases: An observational study on 2010 patients Lavinia Domenici, Italy
10:56-11:04	OP1-205 The modern Catholic church and contraception – Starting a dialogue about rethinking the church's position on contraception Jan Gregus, Czech Republic
11:04-11:13	OP1-206 Prevalence of pelvic floor dysfunction symptoms in reproductive age women Natalia Artymuk, Russia
11:13-11:22	OP1-207 Conservative treatment of cervical ectopic pregnancy: Methotrexate vs uterine artery embolization Andrey Kozachenko, Russia
11:22-11:31	OP1-208 New theory of normal and deviant uterovaginal embryogenesis Zograb Makiyan, Russia
11:31-11:40	OP1-209 Supplementation of granulocyte-macrophage colony-stimulating factor to culture medium might rectify pregnancy rates in patients having history of failed IVF due to embryo development arrest Mehmet Sipahi, Turkey
11:40-11:50	OP1-210 Ulipristal acetate inhibits leiomyoma cell growth via TGF- β signaling pathway Gabriela Sokolowska, Poland

11:50-12:10 BREAK

12:10-13:40	ORAL PRESENTATION 3 – FETOMATERNAL MEDICINE	ABBEY
Chairpersons	Mattheos Fraidakis, Greece Isaac Blickstein, Israel	
12:10-12:19	OP1-301 Pregnancy outcomes in rheumatic diseases: A single center experience Catarina Ambrósio, Portugal	
12:19-12:28	OP1-302 Successful emergency cerclage at nine weeks gestation in woman with habitual abortions and intrauterine adhesions Eiman Shalabna, Israel	
12:28-12:37	OP1-303 Pregnancy outcomes after large loop excision of the transformation zone – Is it really that risky? Rita Mamede, Portugal	
12:37-12:46	OP1-304 Maternal dietary patterns during pregnancy and offspring size at birth: A systematic review of the evidence Camilla Nykjaer, UK	



SATURDAY, NOVEMBER 24, 2018

12:46-12:55	OP1-305 Efficacy and safety of isoxsuprine hydrochloride as uterine relaxant in preterm labor - A prospective, open-label, non-comparative study (First analysis results) P B Jaju, India
12:55-13:04	OP1-306 Preliminary results from the nationwide Austrian register for reproduction and rheumatic disease (RHE Pro register) Klara Rosta, Austria
13:04-13:13	OP1-307 Maternal serum matrix metalloproteinase 14 (MMP14) in preeclampsia and normal pregnancy women: Alternative biomarker of preeclampsia Herman Sumawan, Indonesia
13:13-13:22	OP1-308 Alternative approaches to surgical hemostasis in patients with morbidly adherent placenta undergoing fertility-sparing surgery Roman Shmakov, Russia
13:22-13:31	OP1-309 Active versus expectant management in women with severe preeclampsia Roman Shmakov, Russia
13:31-13:40	OP1-310 Low maternal concentrations of human chorionic gonadotropin (hCG) in early pregnancy: An indicator of increased risk of adverse pregnancy outcome? Anne Eskild, Norway

13:40-14:30
LUNCH BREAK AND POSTER VIEWING
EXHIBITION AREA

14:30-16:30	ORAL PRESENTATION 4 – GYNECOLOGY	ABBEY
Chairperson	Xavier Bosch, Spain Efraim Siegler, Israel	
14:30-14:38	OP1-401 Detection of human papilloma virus and Epstein Barr virus in squamous cell carcinoma of the cervix Mohamed Abdelrahman, Ireland	
14:38-14:46	OP1-402 Human papillomavirus detection in self-sampling versus clinician-collected samples of vaginal discharge: Efficiency, acceptability and predictive value Tatiana Belokrinitskaya, Russia	
14:46-14:54	OP1-403 Vaginal involvement as an independent predictor of outcome in FIGO stage IIB and IIIB carcinoma cervix - A single institutional retrospective study Satadru Biswas, India	
14:54-15:02	OP1-404 First trimester post-abortal placenta increta: A case report Marion Ariadne Burgos, Philippines	
15:02-15:10	OP1-405 Comprehensive multidisciplinary management of malignant ovarian germ cell tumors and fetomaternal outcome: Serial case report Christina Prajawati Ni Luh Lany, Indonesia	

15:10-15:18	OP1-406 Muscle-sparing skin-reducing breast reconstruction with pre-pectoral implants in breast cancer patients: Long term assessment of patients' satisfaction and quality of life Lavinia Domenici, Italy
15:18-15:26	OP1-407 CIN 2-3 in pregnancy -the safety of Lletz in the first 15 weeks and the risk of cervical cancer Efraim Siegler, Israel
15:26-15:34	OP1-408 Risk factors and the appearance of breast cancer Domagoj Krpina, Croatia
15:34-15:42	Op1-409 Recurrence rates after pelvic gynaecologic neoplasms Sinziana Ionescu, Romania
15:42-15:50	OP1-410 High correlation between clearance of HR-HPV types after Lletz in early stage cervical cancer and absence of residual cancer in the final pathological specimen Efraim Siegler, Israel
15:50-15:58	OP1-411 Growing teratoma syndrome following treatment for immature teratoma of ovary – A case report Célia Soares, Portugal
15:58-16:06	OP1-412 Primary cytoreductive surgery or neoadjuvant chemotherapy and interval debulking surgery in advanced ovarian epithelial cancer - Preliminary results in a series of 298 patients George Daniel Subtirelu, Romania
16:06-16:14	OP1-413 Introduction and evaluation of a simplest and fastest cervical cancer screening technology for resources limited area Y. Wang, USA
16:14-16:22	OP1-414 Effects of electric field on endometrial adenocarcinoma cells and autophagy activities Xing Wei, China
16:22-16:30	OP1-415 Prognosis of hormone-dependent breast cancer seems to be influenced by KEAP1, NRF2 and GSTM1 genetic polymorphisms Micaela Almeida, Portugal

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	ORAL PRESENTATION 5 – FETOMATERNAL MEDICINE	ABBEY
Chairpersons	Mattheos Fraidakis, Greece Johannes Bitzer, Switzerland	
16:50-16:58	OP1-501 The association between blood type group and early postpartum hemorrhage Mais Ali-Saleh, Israel	
16:58-17:06	OP1-502 An unusual cause of abdominal pain in a patient with placenta praevia Olivia Anne Cassar, Malta	



SATURDAY, NOVEMBER 24, 2018

17:06-17:14	OP1-503 The evaluation of the first-trimester biochemical parameters of combined aneuploidy screening test in pregnant women with Polycystic Ovary Syndrome (PCOS) Mahbod Ebrahimi, Iran
17:14-17:22	OP1-504 Perinatal outcomes in pregnancies after adenomyomectomy with TOUA, in a single institute Yong-Soon Kwon, South Korea
17:22-17:30	OP1-505 Second trimester ultrasound – Increasing ergonomics and efficiency with a new examination table design Lars Hårleman, Sweden
17:30-17:38	OP1-506 Fertility and pregnancy outcomes in patients with uterine adenomyosis, who have received adenomyomectomy with TOUA in a single institute Yong-Soon Kwon, South Korea
17:38-17:46	OP1-507 Successful outcome of hepatic adenoma rupture on intracytoplasmic sperm injection related pregnancy Renato Martins, Portugal
17:46-17:54	OP1-508 Peripheral natural killer cells in infertile women: Clinical pregnancy rates and miscarriage incidence Boryana Petkova, Bulgaria
17:54-18:02	OP1-509 An analysis of pregnancy perception of pregnant women in terms of stress, demographic and obstetric characteristics Anayit Margrit Coşkun, Turkey
18:02-18:10	OP1-510 Giant cystadenoma in pregnancy: A laparoscopic approach Helena Veloso, Portugal
18:10-18:18	OP1-511 Maternal vitamin d deficiency increases the risk of gestational diabetes: A prospective study Marina Sousa Gomes, Portugal

SUNDAY, NOVEMBER 25, 2018

INFERTILITY/ART/IVF

08:30-10:00	ENDOMETRIOSIS ADENOMYOSIS	FLEMING
Capsule	The debate continues whether mechanical infertility should be treated surgically or medically.	
Chairpersons	Alan DeCherney, USA Victor Gomel, Canada Nikolaos Polyzos, Spain	
08:30-09:15	Debate: Ovarian endometrioma before infertility Prefer IVF first: Edgardo Somigliana, Italy Prefer surgery first: Jacques Donnez, Belgium	
09:15-09:40	Artificial uterus Mats Hellström, Sweden	
09:40-10:00	Uterine adenomyosis: Can surgery help? Leila Adamyan, Russia	

10:00-10:20
COFFEE BREAK AND POSTER VIEWING
EXHIBITION AREA

10:20-11:50	ET AND LUTEAL SUPPORT	FLEMING
Capsule	Implantation is the least effective stage of IVF. The holy grail is to differentiate the many factors involved in implantation and failure. Surely ET and luteal phases support are important, but often there is little evidence with many practices never proven.	
Chairpersons	Edgardo Somigliana, Italy Jacques Donnez, Belgium Aleksandar Stefanović, Serbia	
10:20-10:40	Progesterone support: Are all progesterone's similar? Is there an upper dose for progesterone? Avi Harlev, Israel	
10:40-11:05	Adjuvant luteal support, other than progesterone. Any proofs? Basil Tarlatzis, Greece	
11:05-11:25	Why are we not all TOP-performing in embryo transfer techniques? Mohamed Aboulghar, Egypt	
11:25-11:50	MicroRNAs new generation test to explore implantation window Samir Hamamah, France	

11:50-12:10
BREAK

12:10-13:40	GENETIC TESTING OF EMBRYOS	FLEMING
Capsule	Genetics testing of embryos is increasing. However, the results remain highly controversial. What has been proven to be the value of PGT, rather than what has not? What are we missing when we offer it to all?	
Chairpersons	Simon Fishel, UK Attila Vereczkey, Hungary	
12:10-12:55	Debate: PGT for patients 35 and older: Tony Gordon, UK Only blastocyst transfer, no add ons (no time lapse, no PGT): Pasquale Patrizio, USA	



12:55-13:40	Debate: Mitochondrial DNA (mtDNA) can serve as a biomarker of pre-implantation embryo viability Pros: Dagan Wells, UK Cons: Nathan Treff, USA
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13:40-14:30 LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA

14:30-16:30	IVF: LESS IS MORE?	FLEMING
Capsule	Will we do better with less eggs, less technologies, less testing?	
Chairpersons	Rene Frydman, France Norbert Gleicher, USA Victor Gomel, Canada	
14:30-15:00	Alternatives before IVF Ben Mol, Australia	
15:00-15:30	Risk of cancer in women and children after ART Alastair Sutcliffe, UK	
15:30-16:00	One and done: More or less eggs? What is the best? Samir Hamamah, France	
16:00-16:30	Special COGI-RBMO countercurrent lecture. 40 years on: Moving towards stratifying patient treatment and removing subjectivity from IVF practice Simon Fishel, UK	

16:30-16:50 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	RTD ON PROVEN AND UNPROVEN ART PROCEDURES	FLEMING
Capsule	Panelist - Audience discussion	
Chairpersons	Zion Ben Rafael, Israel Bart Fauser, Netherlands	
Panelists	Frank Broekmans, Netherlands Simon Fishel, UK Norbert Gleicher, USA Samir Hamamah, France Edgardo Somigliana, Italy	
16:50-18:20	What evidence do we have that assisted hatching works? What evidence do we have for stem cell replenishment or ovarian rejuvenation? What evidence do we have for the value of endometrial scratching? What evidence do we have that high dose FSH can increase success in low responders? What evidence do we have that the "only SET policy" will not affect success? How strong are the evidences that in vitro activation of follicles is a viable option for the future? How strong are the evidences that DHEA / testosterone pretreatment can affect IVF results in LR?	



SUNDAY, NOVEMBER 25, 2018

INFERTILITY/ART/IVF II

08:30-10:00	MOSAICISM	WESTMINSTER
Capsule	One of the limitations of PGT is the interpretation of mosaicism. While it was proven that mosaic embryos can be transferred and result in normal babies, the true meaning of the high rate of mosaicism found in PGT remains controversial. In a multilateral debate, the authors will argue two different standpoints.	
Chairpersons	Rita Vassena , <i>Spain</i> Samir Hamamah , <i>France</i>	
08:30-08:50	Selective outcome reporting and sponsorship in randomized controlled trials in IVF and ICSI Fulco van der Veen , <i>Netherlands</i>	
08:50-09:35	<u>Debate:</u> Mosaicism is not an obstacle for PGS to work: Tony Gordon , <i>UK</i> PGS works and mosaicism is overestimated: Nathan Treff , <i>USA</i>	
09:35-10:00	Genomic medicine for personalized IVF/ICSI cycle Samir Hamamah , <i>France</i>	

10:00-10:20
COFFEE BREAK AND POSTER VIEWING
EXHIBITION AREA

10:20-11:50	JOINT COGI-ISMAAR (INTERNATIONAL SOCIETY FOR MILD APPROACHES IN ASSISTED REPRODUCTION) SESSION	WESTMINSTER
Capsule	It is widely accepted that mild stimulation for IVF reduces health risks for women and provides better quality oocytes. This session is dedicated to describing indications and management of natural and mild stimulation IVF cycles including the role of advanced ultrasound in improving outcomes	
Chairpersons	Geeta Nargund , <i>UK</i> Rene Frydman , <i>France</i>	
10:20-10:50	Edwards and Steptoe trust lecture: The birth of the first "Test Tube Baby" in the British press Katie Dow , <i>UK</i>	
10:50-11:20	Natural and mild IVF - When and how to do it Geeta Nargund , <i>UK</i>	
11:20-11:50	The role of advanced ultrasound in improving outcomes in natural and mild IVF Stuart Campbell , <i>UK</i>	

11:50-12:10
BREAK


12:10-13:40	SPECIAL WORKSHOP - HISTORY OF IVF: PART I	WESTMINSTER
Capsule	This session is based on the book "The History of IVF", published recently in celebration of the 40th anniversary of IVF. The authors, all pioneers in their respective countries, will present their experience and discuss the development of IVF from its beginning to a huge interdisciplinary medical field which helps millions of patients, affecting many lives and even spilling over to the assistance of endangered species. Read the book for more and to see the topics and speakers' bios.	
Chairpersons	Gab Kovacs , <i>Australia</i> Peter Brinsden , <i>UK</i>	
12:10-12:35	The early American experience Alan DeCherney , <i>USA</i>	
12:35-12:55	The track to assisted reproduction: Animal to human IVF Jacques Cohen , <i>USA</i>	
12:55 -13:15	The early days in the UK: Steptoe, Edwards, Purdy and Bourn Hall Peter Brinsden , <i>UK</i>	
13:15-13:40	The contributions from "down under" Gab Kovacs , <i>Australia</i>	

13:40-14:30

LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA

14:30-16:30	SPECIAL WORKSHOP - HISTORY OF IVF: PART II	WESTMINSTER
Capsule	Based on the book "The History of IVF", Part II	
Chairperson	Jacques Cohen , <i>USA</i>	
14:30-14:55	Developments in Europe Basil Tarlatzis , <i>Greece</i> Klaus Diedrich , <i>Germany</i>	
14:55-15:20	Development of IVF in India Rina Agrawal , <i>UK</i>	
15:20-15:45	The development of ovarian stimulation protocols for IVF Colin Howles , <i>Switzerland</i>	
15:45-16:10	Research on ART families: An historical perspective Susan Golombok , <i>UK</i>	
16:10-16:30	The commercialization of IVF in the UK Tony Rutherford , <i>UK</i>	



SUNDAY, NOVEMBER 25, 2018

GYNECOLOGY

08:30-10:00	SLS: THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS UPDATES ON THE STATE OF THE ART OF MINIMALLY INVASIVE SURGERY TO PRESERVE FERTILITY	ST. JAMES
Capsule	Endoscopic surgery is expanding and becoming minimally invasive. Where is the limit?	
Chairpersons	Pierluigi Benedetti Panici , <i>Italy</i> Jessica Ybanez Morano , <i>USA</i>	
08:30-08:50	The future of minimally invasive surgery for the infertility patient: Making minimally invasive surgery even less invasive Mona Orady , <i>USA</i>	
08:50-09:10	Surgical management of multi-organ endometriosis and pregnancy outcomes Theirs Soares Raymundo , <i>USA</i>	
09:10-09:35	Radio-frequency ablation: Applications for the preservation of the fibroid uterus Jessica Ybanez-Morano , <i>USA</i>	
09:35-10:00	Dysfunctional uterine bleeding during adolescence George Creatsas , <i>Greece</i>	

10:00-10:20 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

10:20-11:50	GENERATING AN HPV DIAGNOSIS IN A SCREENING EVENT	ST. JAMES
Capsule	Screening programs need to decide on the technologies employed and usually reply on lab decisions. However, clinicians would benefit from better understanding the subtleties of HPV diagnostics.	
Moderator	Xavier Bosch , <i>Spain</i>	
Participants	Jorma Paavonen , <i>Finland</i> Mario Poljak , <i>Slovenia</i>	
Questions	Sampling and self-sampling HPV tests interferences: Blood / Infections HPV testing: Sensitivity and specificity of the test The value of type specific testing: Cocktail vs. some types vs. all types Multiple HPV infections: What do they convey as a predictor of risk? Co testing: The obvious and the uncertain Other	

11:50-12:10 BREAK



12:10-13:40	HPV VACCINES: LIGHTS AND SHADOWS	ST. JAMES
Capsule	In Europe, as well as in some developing countries, non-scientific claims of serious adverse events following vaccination are challenging public programs and undermining vaccine confidence.	
Moderator	Xavier Bosch , <i>Spain</i>	
Participants	Elmar Joura , <i>Austria</i> Pauline Paterson , <i>UK</i> Jorma Paavonen , <i>Finland</i>	
Questions	What is vaccine hesitancy? Vaccine safety: The weight of the evidence The creation and spreading of a rumor: Impact on public programs Mandatory vaccination How to confront vaccine hesitancy and anti-vaccine positions Other	

13:40-14:30

LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA

14:30-15:00	INDUSTRY SUPPORTED LECTURE	ST. JAMES
Chairpersons	Mark Brincat , <i>Malta</i> Marco Gambacianni , <i>Italy</i>	
14:30-15:00	<i>Industry supported Special Lecture – See page 155</i>	
15:00-16:30	PREMATURE OVARIAN FAILURE	ST. JAMES
15:00-15:25	Gene involvement in menopause and POI Joop Laven , <i>Netherlands</i>	
15:25-15:50	Women with a family history of POI should be offered fertility preservation Claus Yding Andersen , <i>Denmark</i>	
15:50-16:30	<u>Debate: Should androgens be routinely offered to optimize quality of life in menopause?</u> For: Alessandra Graziottin , <i>Italy</i> Against: Johannes Bitzer , <i>Switzerland</i>	

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	MENOPAUSE AND PERIMENOPAUSE	ST. JAMES
Chairpersons	Johannes Bitzer , <i>Switzerland</i> Marco Gambacianni , <i>Italy</i>	
16:50-17:10	Non-hormonal vs hormonal treatment for the menopause. Time to rethink, again? Mark Brincat , <i>Malta</i>	
17:10-17:35	Microbiome in menopause or in relation to hormone levels Gary Ventolini , <i>USA</i>	
17:35-17:55	Perimenopausal contraception: What are the options? Alessandra Graziottin , <i>Italy</i>	
17:55-18:20	Optimizing psychosexual health with perimenopausal contraception Johannes Bitzer , <i>Switzerland</i>	



SUNDAY, NOVEMBER 25, 2018

FETOMATERNAL MEDICINE

08:30-10:00	PRENATAL DIAGNOSIS AFTER ASSISTED REPRODUCTION	WHITTLE
Capsule	Are recommendations after ART different?	
Chairpersons	Gian Carlo Di Renzo , <i>Italy</i> Maria Gil , <i>Spain</i>	
08:30-08:55	Non-invasive prenatal testing in twins Maria Gil , <i>Spain</i>	
08:55-09:20	NIPT in the context of IVF and PGS Francesca Grati , <i>Italy</i>	
09:20-10:00	Special lecture: Prenatal screenings after ART Kypros Nicolaides , <i>UK</i>	

10:00-10:20 COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

10:20-11:50	PREVENTION OF PREMATURE BIRTH	WHITTLE
Capsule	One of major risks of pregnancy is premature birth, which prevention steps can we offer?	
Chairpersons	Ben Mol , <i>Australia</i> Yariv Yogev , <i>Israel</i>	
10:20-10:45	Pessary in the prevention of preterm birth Ben Mol , <i>Australia</i>	
10:45-11:05	Previous PTL: How should we treat the index pregnancy? Andrew Shennan , <i>UK</i>	
11:05-11:30	The contribution of twins conceived by assisted reproduction technology to the very preterm birth rate: A population-based study Isaac Blickstein , <i>Israel</i>	
11:30-11:50	How to treat twins with cervical shortening? How to treat a pregnancy after previous PTL? Andrew Shennan , <i>UK</i>	

11:50-12:10 BREAK

12:10-13:40	PREDICTION, PREVENTION MANAGEMENT OF PREECLAMPSIA	WHITTLE
Capsule	For over 3 decades the effort to predict and prevent preeclampsia continues: Are we on the verge of success?	
Chairpersons	Kypros Nicolaides , <i>UK</i> Andrew Shennan , <i>UK</i>	
12:10-13:00	Special lecture: Prediction and prevention of preeclampsia Kypros Nicolaides , <i>UK</i>	
13:00-13:20	Maternal hemodynamics in patients with preeclampsia Asma Khalil , <i>UK</i>	
13:20-13:40	Management of hypertension in pregnancy Laura Magee , <i>UK</i>	

13:40-14:30 LUNCH BREAK AND POSTER VIEWING

EXHIBITION AREA



14:30-16:30	HOT CONTROVERSIES	WHITTLE
Chairpersons	Dan Farine , <i>Canada</i> Asma Khalil , <i>UK</i>	
14:30-14:55	Placenta percreta clinic Ally Murji , <i>Canada</i>	
14:55- 15:20	What is new in HIV Mark Yudin , <i>Canada</i>	
15:20-15:45	Biomarkers for preterm birth: Vaginal cytokines and lactobacilli species Gary Ventolini , <i>USA</i>	
15:45-16:00	Erbium laser treatment for episiotomy scars Aleksandra Novakov-Mikic , <i>Serbia</i>	
16:00-16:30	Special countercurrent lecture: Fetal ultrasound size charts do more harm than good at term Basky Thilaganathan , <i>UK</i>	

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	GESTATIONAL DIABETES AND OBESITY	WHITTLE
Capsule	Hot controversies in GDM and obesity	
Chairperson	Basky Thilaganathan , <i>UK</i>	
16:50-17:20	Debate: Should we preform antenatal surveillance in GDM? Intensive, non-intensive not at all? Pro treatment: Dan Farine , <i>Canada</i> Con: Gerard Visser , <i>Netherlands</i> Discussion	
17:20-17:50	Debate: Oral hypoglycemic agents: It's time for a consensus Pro: Yariv Yogev , <i>Israel</i> Con: Gerard Visser , <i>Netherlands</i> Discussion	
17:50-18:20	Debate: Should we treat and who should treat obesity during pregnancy? Yes, and in dedicated clinic: Dan Farine , <i>Canada</i> No, it's ineffective and not important: Yariv Yogev , <i>Israel</i> Discussion	



SUNDAY, NOVEMBER 25, 2018

ORAL PRESENTATIONS

08:30-10:00	ORAL PRESENTATION 1 – FETOMATERNAL MEDICINE	ABBEY
Chairpersons	Katerina Jeremic , <i>Serbia</i> Gerard Visser , <i>Netherlands</i>	
08:30-08:37	OP2-101 Endovascular Management of Intrapartum Accreta: A Useful Uterus-Preserving Technique for Future Fertility Abdulwahab Al Jabari , <i>Saudi Arabia</i>	
08:37-08:44	OP2-102 Effect of antenatal education and counseling to fear of childbirth and childbirth attitudes in nulliparous pregnant women Burcin Bektas Pardes , <i>Turkey</i>	
08:44-08:51	OP2-103 Consent in caesarean section – Are we doing it right? Miriam Duncumb , <i>UK</i>	
08:51-08:58	OP2-104 Blood loss, massive transfusion and hemoglobin levels in patients undergoing emergency peripartur hysterectomy at a German tertiary perinatal care unit during the last 13 years Florian Ebner , <i>Germany</i>	
08:58-09:05	OP2-105 Evaluation of perioperative practices according to eras protocol in elective cesarean surgery Fulden Ozkececi , <i>Turkey</i>	
09:05-09:12	OP2-106 Does intrahepatic cholestasis of pregnancy present differently in in vitro fertilization versus spontaneous pregnancies? Eiman Shalabna , <i>Israel</i>	
09:12-09:19	OP2-107 Trauma, violence, and birth: Communion and agency in narratives of diverse birth experiences Hannah Tello , <i>USA</i>	
09:19-09:26	OP2-108 Effects of corticosteroids on cardiovascular function of fetuses with growth restricted Homeira Vafaei , <i>Iran</i>	
09:26-09:33	OP2-109 Loss of X chromosome inactivation in monospermic complete hydatidiform moles with 46, XX karyotype. Lingfang Wang , <i>China</i>	
09:33-09:40	OP2-110 Intraplental villous artery doppler as an independent predictor for placenta mediated disease and its comparison with uterine artery doppler and/or placental biochemical markers: A prospective cohort study Inas Babic , <i>Saudi Arabia</i>	
09:40-09:47	OP2-111 Pregnancy and birth at woman born with gastroschisis Ana Marija Stojic , <i>Croatia</i>	
09:47-09:54	OP2-112 The concentrations of Placental Growth Factor and Endoglin in pregnancy complicated by pre-eclampsia Dorota Darmochwal-Kolarz , <i>Poland</i>	

10:00-10:20
COFFEE BREAK AND POSTER VIEWING
EXHIBITION AREA

10:20-11:50	ORAL PRESENTATION 2 – INFERTILITY/ART/IVF	ABBEY
Chairperson	Aleksandar Stefanović, Serbia	
10:20-10:29	OP2-201 Incidence of chromosomal aneuploidies at embryonic level with comparison based on maternal age Natalia Aleksandrova, Russia	
10:29-10:38	OP2-202 Frozen embryo transfer after PGT-A cycles: Wait or not wait? Cerrillo Maria, Spain	
10:38-10:47	OP2-203 A cost-effectiveness evaluation comparing originator r-hFH, biosimilar r-hFSH and u-hFSH in women undergoing ovarian stimulation for ICSI Carmelo Cimino, Italy	
10:47-10:56	OP2-204 distribution of mthfr isoforms carriers and level of homocysteine in an infertile population with assisted reproductive technologies (ART) cycle failures Arthur Clement, France	
10:56-11:05	OP2-205 Influence of genital infections in women with recurrent implantation failure on IVF outcomes Joon Cheol Park, South Korea	
11:05-11:14	OP2-206 Comparison of pregnancy outcomes in patients undergoing intrauterine insemination (IUI) following ovulation induction by letrozole versus clomiphene citrate Kanika Ranjan, India	
11:14-11:23	OP2-207 diminished ovarian reserve in a newly diagnosed breast cancer patient with heterozygote ataxia telangiectasia mutated (ATM) gene mutation Gulnaz Sahin, Turkey	
11:23-11:32	OP2-208 Double vitrification cycles yield higher pregnancy rates than fresh cycles and one-vitrification cycles Sofia Soto Rodriguez, Mexico	
11:32-11:41	OP2-209 Knowledge and opinions of midwifery and nursing students concerning oocyte cryopreservation Ozden Tandogan, Turkey	
11:41-11:50	OP2-210 Testis Regenerative Matrix (TREM) bioexpansion in Testis Insufficiency Syndrome (TIS) <i>Testis Expandable BioSurgery and MicroSurgery (TEBS and TEMS) in Male Infertility based on Autologous Regenerative Stem Cells</i> Giuseppe Tritto, Italy	

11:50-12:10 BREAK

12:10-13:40	ORAL PRESENTATION 3 – INFERTILITY/ART/IVF	ABBEY
Chairperson	Victor Gomel, Canada	
12:10-12:19	OP2-301 Distribution of MTHFR isoforms carriers and level of homocysteine in an infertile population with assisted reproductive technologies (ART) cycles failures Arthur Clement, France	



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12:19-12:28	OP2-302 Genetic screening in patients with recurrent pregnancy loss Anastasiia Syrkasheva, Russia
12:28-12:37	OP2-303 Impact of PTEN inhibition and low dose rapamycin on primordial follicles activation and DNA damage response of bovine ovarian follicles in vitro Mila Maidarti, UK
12:37-12:46	OP2-304 Lypid Disregulation in seminal and follicular fluids could affect gonadal response Rocio Nuñez Calonge, Spain
12:46-12:55	OP2-305 Endometrial and myometrial vascularity as predictors of implantation outcome Chadi Fakih, Lebanon
12:55-13:04	OP2-306 Genetic screening results of women who underwent IVF treatment according to their IVF indication: Single center experience Nafiye Karakas Yilmaz, UK
13:04-13:13	OP2-307 Investigation of the role of serum telomerase levels in patients with occult primary ovarian insufficiency Duygu Tugrul Ersak, Turkey
13:13-13:22	OP2-308 Improved vitrification method yields to the highest worldwide positive pregnancy outcomes compared to fresh cycles Sofia Soto Rodriguez, Mexico
13:22-13:31	OP2-309 Isoleted teratozoospermia doesn't negatively impact fertilization, embryo development and implantation rates when using intracytoplasmic sperm injection (ICSI) vs in vitro fertilization (IVF) as an insemination method Jorge Alberto Macías González, Mexico

13:40-14:30
LUNCH BREAK AND POSTER VIEWING
EXHIBITION AREA

14:30-16:30	ORAL PRESENTATION 4 – FETOMATERNAL MEDICINE	ABBEY
Chairpersons	Asma Khahil, UK Linda Harel, Israel	
14:30-14:40	OP2-401 Maternal obesity and rectovaginal group B Streptococcus colonization at term Joana Pereira, Portugal	
14:40-14:50	OP2-402 Is the IADPSG screening for gestational diabetes better than the two-step strategy in the detection of diabetes or glucose intolerance in postpartum? Elena Costa, Belgium	
14:50-15:00	OP2-403 Hypnosis in childbirth Linda Harel, Israel	
15:00-15:10	OP2-404 Fetomaternal medicine department admissions in a tertiary care hospital Maria Moleiro, Portugal	



15:10-15:20	OP2-405 Postpartum mystery- Tuberculosis Annanyaa Raya Reddy, India
15:20-15:30	OP2-406 Determining the self-care agency and the health practice levels of the pregnant women and the effective factors Asli Sis Celik, Turkey
15:30-15:40	OP2-407 Successful non-surgical management of second trimester heterotrophic abdominal pregnancy Samina Zafar, Pakistan
15:40-15:50	OP2-408 The effects and related factors of health literacy status and self-efficacy of pregnant women Sema Dereli Yilmaz, Turkey
15:50-16:00	OP2-409 Do patients take responsibility for their own safety? A questionnaire-based survey in a multi-ethnic north London population Zouina Assassi, UK
16:00-16:10	OP2-410 The role of chemoradiation in locally advanced cervical cancer Rajeev Singh, Australia
16:10-16:20	OP2-411 Sequential cervical ripening - Worthwhile procedure or double trouble? Mirit Toledano Hacoen, Israel

16:30-16:50

COFFEE BREAK AND POSTER VIEWING

EXHIBITION AREA

16:50-18:20	ORAL PRESENTATION 5 - GYNECOLOGY	ABBEY
Chairperson	Gary Ventolini, USA	
16:50-16:59	OP2-501 Immediate postoperative pain control with ropivacaine following laparoscopic-assisted vaginal hysterectomy: A randomized double-blind, pilot study Jae Young Kwack, South Korea	
16:59-17:08	OP2-502 Identification and characterization of human ovary-derived circular RNAs and their potential roles in ovarian aging Hongcai Cai, China	
17:08-17:17	OP2-503 The effect of the hot flash problem experienced during menopause on complementary alternative medicine attitudes and health beliefs Dilek Coşkuner Potur, Turkey	
17:17-17:26	OP2-504 Is ovarian cystic lesion is the most fruitful pathology in the female infertility? A single tertiary care center experience Poonam Yadav, India	
17:26-17:35	OP2-505 The effect of sufficient and insufficient vitamin E in treatment of infertile PCOS patients Athar Rasekh Jahromi, Iran	
17:35-17:44	OP2-506 The follicular environment and oocyte quality of women with ovarian endometriosis: Nuclear factor KAPPA B and telomerase of granulosa cells Ying Li, China	



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17:44-17:53	OP2-507 Correlation of visual (modified Ferriman Gallway scoring) and biochemical evaluation of hirsutism in polycystic ovary syndrome Filipino patients in UERMMMC: A cross sectional study Marth Louie Tarroza, Philippines
17:53-18:02	OP2-508 Urinary incontinence in pregnancy: A literature review Sema Dereli Yilmaz, Turkey
18:02-18:11	OP2-509 Do the angiogenic and haemostatic profiles depend on tumour's localisation in invasive breast cancer? Elzbieta Zarychta, Poland





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Abstracts



INVITED SPEAKER ABSTRACTS

WHY ARE WE NOT ALL TOP-PERFORMING IN EMBRYO TRANSFER TECHNIQUES?

Mohamed Aboulghar

Professor, Cairo University, Cairo, Egypt; Clinical Director, The Egyptian IVF Center, Cairo, Egypt

Embryo transfer is the final and most critical step in the IVF. For the success of IVF the embryo should be delivered in the proper place in the uterus atraumatically.

Objectives: To explain the difficulties we may face during embryo transfer and how to avoid them including methods to avoid initiation of uterine contraction during the procedure and the possible use of different embryo transfer catheters, and ultimately to find out the best technique for embryo transfer.

Negative factors that can affect ET:

- (i) initiation of uterine contractility that may lead to expulsion of the embryos;
- (ii) the presence of cervical mucus that can plug the tip of the catheter or entangle the embryos and drag them out during withdrawal of the catheter;
- (iii) proper placement of the embryos into the uterine cavity may not be achieved due to failure to pass the catheter through the internal os. This can be due to acute utero-cervical angulation, cervical stenosis or anatomical distortion of the cervical canal.

Procedures to improve performance in ET: Ultrasonography gives precise information about the length of the uterine cavity and the cervical canal and a description of cervical angulations. Catheters should be soft to avoid any trauma to the endocervix or endometrium. The tip of the catheter should not touch the uterine fundus. Depositing the embryos in the mid-fundal area of the uterus improved the pregnancy rate. Gentle manipulation should be the rule. Uterine contractions monitored during embryo transfer were monitored by digital ultrasound and the number of contractions per minute increased as pregnancy rate decreased. Rough manipulation and pulling the cervix initiate strong contractions. The contamination of ET catheter with intravaginal progesterone significantly impaired mouse embryo development and may have an effect on the IVF outcome in the human. The interval between catheter loading and the discharge of the embryos into the uterine cavity affected the IVF outcome, when this delay was greater than 120 seconds there was a decrease in the pregnancy rate. The degree of difficulty of embryo transfer has a negative impact on the live birth rate. Instrumentation, as the use of a tenaculum, reduced the pregnancy rate. Easy embryo transfer was associated with a higher pregnancy rate. Straightening the utero-cervical angle can be achieved by a full bladder before embryo transfer. The use of US guidance for embryo transfer was found to be simple and reassuring and significantly improved pregnancy rates. It lowered the incidence of difficult transfers and confirmed the right placement in the right part of the fundus and minimized contamination of the catheter tip with blood and mucus.

Impact of physician factor: The pregnancy rate after ET depends on the provider. Training for providers improved the performance of ET and improved pregnancy rate.

Studies failed to demonstrate a clear improvement in ongoing pregnancy with bed rest. There is no proof that any adjuvant compounds can have an impact on the outcome of ET.

THE WOMAN TRIAL OF TRANEXAMIC ACID FOR PPH TREATMENT

Sabaratnam Arulkumaran

Emeritus Professor of Obstetrics & Gynaecology, St. George's University of London; on behalf of WOMAN trial collaborators; C/O Clinical Trials' Unit, London School of Hygiene and Tropical Medicine, UK

Of the 300,000 women dying at childbirth every year, 25% are attributed to postpartum haemorrhage. Globally 75,000 women die of PPH every year. But several hundred thousand suffer the consequence of PPH – e.g. hysterectomy, ICU admission, blood transfusion, prolonged hospital stay and anaemia. The WOMAN trial is an international, multi-centre trial that studied the effect of TXA on death, hysterectomy, thromboembolic events and other interventions for post-partum haemorrhage. Tranexamic acid (TXA) is an inexpensive, heat stable, generic drug that reduces bleeding by inhibiting the breakdown of fibrinogen and fibrin. TXA used in surgery show that it reduces bleeding by about one third and when given soon after traumatic injury, it reduces deaths due to bleeding by a third (CRASH-2 trial). The 'WOMAN trial' was an extension of this hypothesis to see reduction of maternal deaths due to PPH with TXA. 20,060 women were randomised to get placebo or Tranexamic acid 1 gm IV when excessive bleeding was noticed. This was in addition to the standard medications (prophylactic and therapeutic oxytocin/ prostaglandins) given during such episode and needed surgical intervention (balloon tamponade/ compression sutures). If bleeding continued for >30 mins or stopped and restarted bleeding within 24 hours, another 1 gm dose was given. Death due to bleeding was significantly reduced in women who had TXA (155 of 10,036 women or 1.5%) compared with those who had placebo (191 of 9985 women or 1.9%). The relative risk (RR) was 0.81 (95% CI 0.65-1.0). If the treatment was given within 3 hours of giving birth, the RR was 0.69 with a 95% CI of 0.52 to 0.91 (p=0.008) i.e. a 30% reduction of maternal deaths due to bleeding and the maximal benefit was seen in those cases with bleeding due to uterine atony. There were other causes of smaller number of maternal deaths, but they were not different between the placebo Vs TXA group. The hysterectomy rates were not different between the two groups. One reason could be the ready recourse to hysterectomies for fear of inability to get adequate quantities of blood for transfusion. The need for repeat surgery for bleeding was reduced by 35% in the TXA group. Thrombo-embolic episodes on the arterial and venous side of the circulation was seen in small numbers but were equal in the placebo and TXA arms of the trial. Based on this trial, a 30% reduction of maternal death can be achieved by implementing a policy of early use of TXA in all cases of PPH.

Recommended reading:

WOMAN trial collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with postpartum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Published online April 26, 2017.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(17\)30638-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)30638-4/fulltext)

WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage. WHO 2017.

<http://www.who.int/reproductivehealth/publications/tranexamic-acid-pph-treatment/en/>



EPIGENETICS AND ART

Jordana Bell

Department of Twin Research and Genetic Epidemiology, King's College London, UK

Background: As the frequency of assisted reproductive technology (ART) treatment increases worldwide, much research has focused on exploring both short and long-term health outcomes associated with conception via ART. Low birth weight, preterm birth, perinatal mortality, congenital malformations, placental complications, and increased frequency of imprinting disorders such as Angelman syndrome and Beckwith-Wiedemann syndrome have been associated with ART; but parallel efforts also report that these associations are not attributed to ART treatment itself, but to multiple pregnancy or parental subfertility, both common factors in ART births. Further research is needed to identify potential factors associated with conception via ART, including not only health outcomes, but also biological consequences such as epigenetic modifications. Epigenetic mechanisms are considered possible mediators of the developmental origins of health and disease, therefore an assessment of the influence of ART on epigenetic profiles may give some insights into mechanisms underlying potential related health outcomes. The association of in vitro fertilisation (IVF) and epigenetic variation has been studied predominantly by exploring DNA methylation at regulatory regions of imprinted genes and at just a few thousand of the ~28 million CpG sites in the human genome. **Hypothesis and methods:** Since IVF procedures are carried out during an important period of epigenetic reprogramming in early development, we hypothesised that IVF may induce epigenetic differences that persist to birth. We interrogated evidence for differential methylation between IVF and non-IVF new-born twins in a comprehensive manner by conducting epigenome-wide association scans (EWAS) using methylated DNA immunoprecipitation followed by deep sequencing (MeDIP-seq). MeDIP-seq genome-wide methylome profiling was carried out in samples from cord blood, and its mononuclear fraction, collected at birth from IVF and non-IVF twins. The use of twins in this study allowed the partition of the observed variance in DNA methylation into genetic and environmental factors. The approach also avoids potential spurious associations due to an imbalanced number of multiple and single pregnancies between conception method groups. Altogether, we investigated the links between IVF and DNA methylation patterns in whole cord blood (n=98) and cord blood mononuclear cells (n=82) from new-born twins. **Results:** We identified one genome-wide significant (genome-wide false discovery rate (FDR) of 5%) whole blood DNA methylation change linked to conception via IVF, which was located ~3kb upstream of TNP1, a gene previously linked to male infertility. The 46 most strongly-associated signals (genome-wide FDR of 25%) included a second region in a gene also previously linked to infertility, C9orf3, suggesting that our findings may in part capture the effect of parental subfertility. Twin-based analyses indicated that individual-specific environmental factors appear to be the main overall contributors of methylation variability at IVF-associated differentially methylated regions, although evidence for methylation heritability was also obtained at several of these regions. We replicated previous findings of differential methylation associated to IVF at the H19/IGF2 region in cord blood mononuclear cells, and we validated the signal at C9orf3 in monozygotic twins. We also explored the impact of intracytoplasmic sperm injection for potential effects specific to male or female infertility factors. **Conclusions:** In a comprehensive study of DNA methylation profiles at birth and IVF conception we show evidence for epigenetic modifications that may in part reflect parental subfertility. The inclusion of twin-only pregnancies also avoided biases present in studies that consider single and multiple pregnancies together. Multiple pregnancies are more common after IVF. Therefore, the differences observed

when studying singleton and twin births together may be confounded with the higher risks of adverse perinatal outcomes in multiple pregnancy births, rather than IVF itself. Nevertheless, we were unable to dissect whether methylation changes were likely caused by IVF, or were due to the underlying parental subfertility, or other factors. These scenarios require further study exploring the stability of the signals over time, their relation with gene expression, and their potential role in health and disease.

Citation Castillo-Fernandez JE, Loke YJ, Bass-Stringer S, Gao F, Xia Y, Wu H, Lu H, Liu Y, Wang J, Spector TD, Saffery R, Craig JM, and Bell JT. 2017. DNA methylation changes at infertility genes in new born twins conceived by in vitro fertilisation. *Genome Medicine*, 9:28.

FREEZING FOR SOCIAL MOTIVES IS NOT COST EFFECTIVE FOR SOCIETY!

Zion Ben-Rafael, MD

Department of Ob/Gyn, Ivf Unit, Laniado, Israel

Delayed childbearing in affluent countries and the financial crisis of the Y-generation contribute to the dramatic decline in birth rate. Social oocyte freezing (SOF) has fueled the imagination of patients and doctors to offer it as a solution to single, presumably fertile, women to preserve their fertility potential by egg banking at an early age. Some are calling on governments to support large scale "fertility preservation", but is it cost-effective? SOF is a kind of 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. However, maximal possible utilization of the frozen eggs is much lower. Until age 35 is only 3%! While freezing between 35-40 the maximal usage rate is 24%! If opting for a partner is set as a condition to usage, than the maximal usage rate becomes extremely low. Recent studies found that only of 3.1%-9.3%, of women returned to use the frozen eggs, which sets the cost of each extra live birth at >\$600,000-1,000,000 or even more, a heavy cost for the society. As IVF is being privatized and business-driven it is hard for experts to decipher scientific from business-oriented claims. The cost-effectiveness of SOF for individuals or society is far from being stated. These facts put the burden of responsibility on the treating physician, who should inform the patients about the true extremely low likelihood of utilizing their eggs- especially if frozen at early age - the age at which to freeze and the possible alternative of oocytes donation if fail to conceive at later age.

OPTIMISING PSYCHOSEXUAL HEALTH WITH PERIMENOPAUSAL CONTRACEPTION

Johannes Bitzer, Switzerland

Sexual health is a comprehensive positive concept of being able to express one's sexual identity, sexual preferences and enjoy sexual pleasure in a safe way and being protected against unwanted pregnancies, STIs and sexual violence. The state of sexual health in the individual is determined by the interaction of biological, psychological and social factors. In the perimenopause are still exposed to a pregnancy although lower than at younger age. The prevalence of STIs seems to increase in this age group due to divorce and new partners. The most frequent problems and dysfunctions are loss of interest in sexual activity and arousal difficulties frequently accompanied by partner conflict. This is also an age group in which the prevalence of pain in the context of sexual activity increases compared to middle aged women. Non-hormonal contraceptives like Copper IUD protect very effectively against unwanted pregnancies, not against STI and the possible negative impact on sexual health may be indirectly via heavy



menstrual bleeding or painful menses. The impact of hormonal contraceptives varies very much between individuals. Potential benefits of CHC are regularisation of the cycle, diminution of hot flushes, positive effect of estrogen on mood and vaginal health. Potential negative effects are the estrogen induced diminution of free testosterone and other side effects. Progestogen only contraception does not reduce free testosterone and has not shown to reduce desire. The impact on mood varies among individuals and progestins. Androgenic progestins seem to have a more negative impact.

LASER TREATMENT OF LICHEN SCLEROSUS ET ATROPHICUS AND PELVIC ORGAN PROLAPSE

Urska Bizjak-Ogrinc, Sabina Sencar
Juna Clinic, Ljubljana, Slovenia

Background and Objective: The purpose of this lecture is to report about newly proposed minimally invasive laser thermo-therapies for lichen sclerosis (LS) and pelvic organ prolapse (POP). **Methods:** We are presenting two prospective studies performed in our clinic. In the first study we were evaluating the laser therapy for lichen sclerosis and atrophicus while in the other we used ER:YAG laser to treat pelvic organ prolapses of higher grade (II and larger). Prior to treatment all patients were clinically inspected, and lichen diagnosis was verified with histological findings. Prolapses were graded with Baden-Walker scale. Patients received three treatment sessions (for LS) and three to five sessions for prolapses. Intervals in between the sessions were 14 days for LS and 2 months for POP. Treatment discomfort was measured at every session with 10-point numerical pain scale. Follow-ups with repeated measurements were performed at 1, 3 and 6 months for LS and 2, 6 and 12 months for POP. **Results:** In LS study 40 patients were randomized into study (laser) group and control (corticosteroid) group with 20 patients each. All 20 patients from laser and 19 patients from control group completed the treatments and were followed up for 1, 3 and 6 months (laser group) and for 1 and 3 months (control). VAS score for dyspareunia in laser group changed from 6.60 to 0.55 (1 mo), 0.50 (3 mo) and 1.88 (6 mo), while itching score went from 7.15 to 1.05, 0.75 and 1.81, respectively. Treatment discomfort was very low (average score of 1.5). Control group had dyspareunia reduced from 5.50 to 2.64 (1 mo) and 3.27 (3 mo). Similarly itching in control group reduced during the treatment from 8.56 to 4.79 (1 mo) and 5.47 (3 mo). Blind assessment of before and after clinical pictures made by two independent evaluators showed statistically significant difference (chi-square=4.47, p=0.035) between groups – there were 75% of correct answers in laser group and 36% in control group. Sexual function significantly improved in laser group (only 10% of patients complained of dyspareunia at 3 mo FU in comparison of 55% at baseline and 15% of anorgasmia vs. 40% at baseline) but not also in control group (dyspareunia: 67% at 3 mo FU and 44% before; anorgasmia: 40% at 3 mo FU and 39% before). Laser treatment discomfort was very low (at Tx1: 0.65, at Tx2: 0.2 and at Tx3: 0.0). The adverse effects were all mild and transient. In prolapse study 61 patients (average age 54.9 yrs, parous status 2.2 and BMI of 25.5) with cystoceles of grades II–IV were treated. Before the treatment there were 40 patients with cystocele of grade II, 15 of grade III and 6 of grade IV. At last follow-up the large majority of patients (58 or 95%) reduced their prolapse grades for at least one grade, 27 of them (44%) for two grades and 8 (13%) even for three grades. At 12 months follow-up 85% of patients had either 0 or I grade of prolapse and the remaining 15% of patients had II grade prolapses. One year after the treatment there were no patients with III or IV grade prolapses. Treatment discomfort was very low (average score of 0.4 on 10 grade scale). There were no adverse effects of this treatment reported. **Conclusions:** Our clinical evaluation of a new non-invasive laser treatments for lichen

sclerosis and pelvic organ prolapses showed efficacy in improvement of LS and POP with no major adverse effects noted. Patients' discomfort during the treatment was minimal and satisfaction very high.

HEALTHY AND SEX STEROID-DEPRIVED VAGINA - FROM PRECLINICAL TO CLINICAL CHARACTERISTICS

Céline Bouchard, Canada

Problem statement: Vulvovaginal atrophy leading to vaginal dryness and secondary dyspareunia affects 50% of postmenopausal women and 72% of women over 70 years of age. The human vagina is composed on three layers, each having specific and different roles. The superficial epithelial layer is responsible for secretion and maintenance of acidic pH, immune response against infection and comfort during intercourse. The second layer is composed of collagen, vessels and some nerve endings. The third (muscular layer) includes nerve endings and is important for the support of the vagina. **Methods and Results:** The response to estrogens or androgens in the different vaginal layers is very different. The thickness of the superficial epithelium secondary to estrogen stimulation has been recognized in many experimental studies. However, data indicate that estrogens decrease the compactness of collagen fibers in the lamina propria without any beneficial effect on nerve endings. In animal models, androgens, as achieved with DHEA (prasterone), which is transformed into both estrogens and androgens, exert a positive action on the three vaginal layers resulting in thickening of the epithelium, lamina propria and muscularis with an increase in nerve ending density. The third muscle layer reacts positively to estrogens and androgens but the development of nerve endings responds to an androgenic action. **Conclusion:** The mechanisms best explaining the positive effects of intravaginal DHEA on sexual dysfunction in women are based on the observation of an increase in vaginal nerve ending density by the androgenic action of DHEA in preclinical models. Further studies are needed to further analyze the specific effect of vaginal DHEA on each human vaginal layer. Studies are also currently underway to evaluate the effect of vaginal DHEA on low sexual desire in women without vaginal atrophy.

CAN HRT AND TREATMENT FOR MENOPAUSE BE INDIVIDUALISED TO REDUCE THE INCIDENCE OF BREAST CANCER

Mark P. Brincat, Malta

Following the publication of the WHI study in JAMA 2001, and all the subsequent instalments right up to the last WHI update in Sept JAMA 2017, it was immediately obvious that in order to maximise benefits in women's health post Menopause, individualisation of therapy was needed. Rather that remains subject to media and marketing forces, proper scientific applications of well-regulated pharmaceuticals demonstrated benefits all cause and maturity in the 18-year WHI follow up and in other publications. In individualising patients, their history, medical and social, as well as their clinical presentation and complaints play a part. In some the short-term symptoms of the immediate post menopause are a problem. In others the long-term problems, of bone loss, cardiovascular disease and objections need to be addressed. Our better understanding of conjugate oestrogens, and oestrogens in general, the difference between natural progesterone and all the different progestogens enable us to be more selective. If used carefully, well-constructed studies have shown consistent reductions in Breast Cancer, whilst improving women's health. Likewise, studies with the various SERMs notably Tamoxifen, Raloxifene and Byrdoxifine have shown increases in bone mass and osteoporotic fractures other benefits and reduction in ER and



breast cancer rates. In patients with cardiovascular disease and metabolic syndrome, both studies have been shown to have a positive impact in reducing breast cancer rates. Thanks to WHI therefore, or despite it we can now be more discerning in dealing with the adult woman's health issues and individualise treatment so as to get a multisystemic maximisation of benefits.

LIGHTS AND SHADOWS IN WHI. A NEVER-ENDING NIGHTMARE

Mark P. Brincat, *Malta*

The story of oestrogen replacement and its variations in menopausal women goes back to the 1930's, but really came to the fore with the work of Robert Greenblatt in the United States and in the UK with the original work of John Studd. The treatment became popular all over the Western World with some areas in the more prosperous areas of the United States registering as many as 50% of the appropriate population being in treatment. The treatment was beneficial to both short term and long-term symptoms of the Menopause. The science was advancing rapidly and the understanding of the function of sex steroids with their nutrisystemic implications getting deeper. All this work came to an abrupt halt with the press releases and later the publication of JAMA of the WHI report in 2001 which suggested but did not in fact show an increase in breast cancer rates attributable to the conjugated oestrogens (CEE) and Medroxyprogesterone acetate CMPA1. The opposite was in fact shown in CEE alone. This publication had a devastating effect on the psyche and use of HRT in postmenopausal women. As a result, women's health was shown to get worse, or at best not improve from the benefits of HRT as one would have hoped. It took 16 years for the final continuous flow of publications from WHI, which were always blurring their original message to demonstrate that overall, even after 18 years after use (average use 5 years to 7 years, CEE and MPA1, CEE respectively, there was a positive effect on mortality, not neutral or negative, from the parameters studies in comparison to placebo. Furthermore, those patients treated in the 50-59-year window which is when most menopause women seek help were the ones to benefit more. What was even more surprising but predicted even from the original WHI study, but not perhaps to this extent was that women on CEE alone experienced a 48%, highly significant reduction in breast cancer. Still the damage is done so the future must lie in proper education on women's health after their menopause. Adult women's health and active healthy aging is priority. The excessive use of HRT has been replaced with more individualised, science based, as opposed to market-based therapy. Also, room for multidisciplinary approach and where necessary, a combination of treatment, possibly more useful than a management alone. Nevertheless, HRT should remain the cornerstone.

Mb/12/10/18

THE EARLY DAYS OF IVF IN THE UK: STEPTOE, EDWARDS, PURDY AND BOURN HALL

Peter R. Brinsden

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"To understand science it is necessary to know its history"
Auguste Comte, 1798 - 1857

The coming together of Patrick Steptoe and Robert Edwards, together with Jean Purdy, in 1968 and their work together over the next ten years culminated in the birth of Louise Brown, the world's first 'Test-tube baby', on the 25th. July 1978. Following this momentous occasion, Steptoe was quoted as saying – 'This is not the beginning of the end, but only the end of the beginning' (Steptoe 1978). They both realised that this was just the

beginning of a whole new clinical and scientific treatment to help infertile couples – about which they were both passionate. However, neither the National Health Service, nor any University, would support their work and they were therefore forced to set up a private clinic. They chose Bourn Hall, the world's first purpose built IVF unit, which opened in September 1980. Soon after Louise Brown was born, other workers, mainly in Australia and the United States, achieved pregnancies in their own units and there was free exchange of clinical and scientific ideas between most of the programmes, with the first World IVF Conference being held at Bourn Hall in 1982. Since these early days, a large number of modifications to the basic IVF treatment have been developed. Techniques for oocyte retrieval have become much easier with the use of vaginal ultrasound, embryo cryopreservation programmes have become standard and several other procedures have been developed, such as intracytoplasmic sperm injection (ICSI), egg and embryo donation, blastocyst culture and preimplantation genetic diagnosis most of which are now part of everyday treatment in IVF units. In the very earliest days of ART, Steptoe and Edwards realised the need for guidelines on many of the ethical issues involving ART. In 1980, the world's first independent Ethics Committee for ART was created at Bourn Hall to help the staff to decide on what were ethically acceptable clinical and laboratory practices, and what should be avoided. Shortly thereafter, the United Kingdom reviewed the whole practice of ART and, in 1984, published the 'Warnock Report'. This is the basis of the legislation that was passed in 1990 as the 'Human Fertilisation and Embryology Act', which, the following year led to the world's first regulatory body for ART – "The Human Fertilisation and Embryology Authority", following which many other countries established their own regulatory processes. Many current ART practices generate controversy, including gamete and embryo donation, surrogacy, sex selection, embryo research, pre-implantation genetic diagnosis and aneuploidy screening, and the treatment of same sex couples. In the future, stem cell research will provide therapeutic options for patients with severely debilitating illnesses that can now only be dreamed of. The early history of IVF is characterised, from the very earliest researchers such as Pincus and Chang through to Steptoe and Edwards, by an absolute dogged determination to succeed in achieving oocytes, embryos, implantation and ultimately healthy live births; initially in animal species and later in humans. We 'lesser mortals' who continue to carry the 'IVF banner' of these early pioneers, and who strive to spread word of the benefits and safety of invitro fertilisation, should learn from the history of ART and the experience of these pioneering 'giants' of our speciality.

WHY STILL USE FSH DOSAGES OVER 225 IU?

Frank J. Broekmans

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Assisted reproduction technology is increasingly applied as a treatment mode for couples with both explained and unexplained infertility. The first step in this treatment is the creation of multiple follicles with the purpose of obtaining the oocytes held within these follicles, creating embryos in the IVF laboratory and replacing the embryos into the uterine cavity. The role for controlled ovarian stimulation as first step relative to the laboratory and transfer phases is not well assessed. How much does it contribute to the final success of the treatment cycle? Research suggests that obtaining a few oocytes less or more is not likely to affect the prospects for the couple. Ovarian stimulation is mostly applied by using exogenous FSH. The response of the ovaries to this exogenous FSH exposure demonstrates a high degree of variation. From a clinical significance point of view the poor ovarian response defined as the yield of less than 5 oocytes is related to an unfavorable prognosis for live birth, although much of this poor prognosis is in fact dictated by female age and not by



the low egg number per se. At the other side of the spectrum, excessive response arbitrarily defined as obtaining more than 15 oocytes at pick up will increase treatment risks for the patient and may even slightly limit the rates of live birth. It is therefore that many clinicians across the world try to foresee the ovarian response category in order to adjust the stimulation protocol with the expectation that the ovarian response can be brought into the normal range (5-15 oocytes), and that by doing so the prospects of pregnancy as well as the safety for the couple will improve.

Prediction of ovarian response category today is mainly applied by using the Antral Follicle Count or Anti-Mullerian Hormone in the early follicle phase. Both relate to the number of antral follicles present at any time and the source for the number of dominant follicles that could grow in results to the application of exogenous FSH. As such, these two ovarian response tests (ORTs) have become the standard test for response prediction, although factors such as female age and possibly body weight may add to this predictive information. It may be noted still that predictions will generally be false positive in some 15% of cases, while only 60-70% of true out of the normal range responders will be identified. Basing the FSH stimulation dosage on such predictions will be imprecise practice from the start. Recent large controlled trials have demonstrated that ORT based individualized dosing of the FSH preparation will not alter the fate of the predicted poor responder but may help in reducing the safety risk of the predicted excessive responder. Unfortunately, the promises of earlier studies that individualized dosing would also affect live birth rates in the ART program as a whole have not been fulfilled. Specifically, in predicted poor responders based on the AMH level, the actual occurrence of a poor response will mean that the couple is in a prognostic unfavorable category. However, using stimulation dosages of over 225 IU will alter the egg number nor the chance of a live birth. So, the combination of low AMH or AFC and subsequently the first cycle poor response may only help to decide whether continuation of the ART treatment is really feasible, but for the purpose of using huge quantities of FSH without any real benefit. A true gain of individualized FSH dosing could be the management of the hyper responding patient. The question then remains whether the AFC will be the prior screening test to select patients to undergo blood sampling for AMH assessment in order to confirm a sufficient risk of excessive response, and to apply reduced FSH dosage or antagonist co-medicated stimulation protocols. We may sincerely consider whether a standard dosage using an antagonist protocol, with the escape of GnRH agonist triggering in case of excessive ovarian response, and with a freeze all strategy as second step, will not be the approach to circumvent imprecise dose picking based on response tests with moderate reliability.

HIGH-THROUGHPUT SINGLE-CELL RNA-SEQ ANALYSIS OF THE ENDOMETRIUM ASSOCIATED WITH RECURRENT PREGNANCY LOSS

Jan Brosens

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In menstruating mammals (humans and higher primates), a critical challenge at implantation is to simultaneously avoid imminent endometrial breakdown and to transform a cycling tissue into a semi-permanent decidua that is maintained throughout pregnancy. While this process is orchestrated by elevated progesterone levels and embryonic cues, it is effected at a tissue level by differentiation of endometrial stromal cells into specialized decidual cells. We used high-throughput single-cell droplet barcoding to profile individual endometrial stromal cell transcriptomes along the decidual pathway *in vitro*. We demonstrate that decidual transformation starts with a precipitous transcriptional response, which is followed by synchronous transition of cells through intermediate states before emerging as

divergent subpopulations, representing mature and acutely senescent decidual cells. We demonstrate that acutely senescent decidual cells are highly inflammatory and that mature decidual cells and uterine NK cells cooperate in eliminating acutely senescent decidual cells through granule exocytosis. We extended our single-cell RNA-seq analysis to timed endometrial biopsies and demonstrate that transition of the endometrium from the mid-luteal receptive phase to the late-luteal refractory (post-receptive) phase is also characterized by progression of stromal cells along diverging lineage trajectories, involving genes with conserved branching dynamics *in vivo* and *in vitro*. Analysis of decidual branching genes in a large number of biopsies revealed that recurrent pregnancy loss is associated with impaired lineage specification of decidual cells.

TIME LAPSE: USEFUL ALGORITHMS OR JUST NICE VIDEOS?

Alison Campbell, UK

Time lapse incubation and monitoring has been gaining popularity over the last decade in human embryology laboratories. This presentation will provide a reminder of the proposed benefits of time lapse imaging in the IVF lab and describe how time lapse data are gathered and used in a clinical setting. Time lapse imaging allows the embryologist to gather detailed information relating to the embryo's *in vitro* development without the need to remove it from its protected culture environment. It also allows each developmental milestone to be logged, giving a precise time line of its development and the ability to scrutinize its morphology by time (morphokinetics). Having a series of images, taken through multiple focal planes, throughout the duration of embryo culture, allows the embryologist to flexibly assess, study and benchmark embryos against each other. It also allows for the pooling of very large datasets and the comparison of morphokinetic timings according to implantation and birth data. This presentation will reference the scientific literature and explore some published, as well as CARE Fertility's, algorithms for embryo selection and consider how useful the time lapse videos can be. This morphokinetic assessment will be compared to standard morphology in terms of subjectivity. A selection of videos will be presented with an explanation of how the time lapse videos can be used very simply to de-select embryos with erroneous cell divisions or behaviors. The use of time lapse videos for more precise assessment of embryos, compared with standard assessment methods will be described. These include accuracy of fertilization assessment, early cleavage events and blastocyst dynamics. A series of novel observations, such as the orientation of polar body extrusion and completion of compaction, which can be used for enhanced embryo selection will be shared. Finally, consideration will be given to what makes a good time lapse algorithm and the types of algorithms available; ranging from integrated software options, to *in house* derived. The experience of the CARE Fertility group will be used to demonstrate that time lapse provides us with far more than simply nice videos and that algorithms can be used to improve outcomes for our patients, compared with standard methodologies.

IVF: THE EARLY AMERICAN EXPERIENCE

Alan H. DeCherney, USA

America has roots in both basic and clinical science. Gregory Pincus, a Harvard professor who helped to establish the Wistar Institute, was primarily a steroid biochemist and responsible for the invention of the birth control pill. He also had a profound interest in reproduction. Working with IC Chang at the Wistar Institute they were able to carry-out the first animal IVF procedures in a rabbit model. He also had a great understanding of sperm,



oocytes and transportation to the fallopian tube. A little-known fact about basic science is that Robert Edwards, based on his friendship with the Jones', worked at Johns Hopkins Institute on basic physiology of the ovary as a young investigator. John Rock, a clinician, also understood the concept of In Vitro Fertilization in the human and wrote about it with various investigators. Rock and Pincus also collaborated on the birth control pill development with Rock carrying-out the clinical piece. The American experience begins clinically with Howard and Georgianna Jones. They left Hopkins after a distinguished career and formerly retired based on age constraints. They moved to Norfolk where their friend Mason Andrews was the Chairmen of the Department and they started their new careers in IVF. They were clearly visionaries. At the same time, they brought Dr. Zev Rosenwaks and Dr. Suheil Muasher to Norfolk to start their successful IVF program. Their great success, besides having superior clinicians, was the employment of Gary Hodgens PhD, who came from the NIH. Hodgens was an exemplary scientist in that he was quickly able to turn scientific questions into answers for clinical questions. At the time that the Norfolk program started, there were four other programs in the United States: Dr. Richard Marrs at USC, Dr. Martin Quigley at the University of Texas, Houston, Dr. Ann Wentz at Vanderbilt, and Dr. Alan DeCherney at Yale. The Norfolk program produced a cadre of "doc's" that have formed IVF centers throughout the world. America had some distinct insights in-regards to IVF. They aggressively looked at ovulation induction, utilizing high dose HMG as opposed to Clomid or natural cycle's and the early use of vaginal ultrasound. Other concepts that grew out of American ideas were surrogacy, GIFT and ZIFT. An important American contribution was the "Culture Club" formed in 1980, utilizing Dr. John Biggars as a mentor, looking at various media improvements. There were an interesting number-of ethical and legal issues associated with IVF. Religious constraints were apparent, but there was also the case of baby M, Dr. Cecil B Jacobson, and the Ricardo Ash Affair. Federal regulation and the Registry were also American spin-off's. America has always been an intellectual leader in developing and pioneering new concepts in IVF and continues to be.

THE LONG WINDING ROAD TO SUCCESS IN ART/ IVF **Alan H. DeCherney, USA**

What Sir Robert Geoffrey Edwards PhD knew and what he did not.

Edwards was an English physiologist who along with Patrick Steptoe, successfully pioneered the concept of In Vitro Fertilization. He trained individuals from around the world and was the founding Editor in Chief of Human Reproduction. In 2010, Edwards was awarded the Nobel Prize in Physiology and Medicine. In 1969 Edwards and Steptoe combined their findings that human eggs could be fertilized by fresh sperm in a petri dish. This resulted from years of work in the laboratory of Dr. Edwards. Steptoe was an equal partner by capturing human oocytes at precisely the right time via laparoscopy. The timing was based on urine testing for the LH surge. That year, in a monumental decision, the British Medical Council rejected an application for research funding of IVF. This resulted in Edwards writing a paper "Social Values and Research in Human Embryology", which was published in nature. The program continued to be supported by the District General Hospital at Oldham and the University of Cambridge. Hormone treatments to stimulate- ovulation failed in their attempts and eventually they reverted to natural cycle IVF. As this is the 40th anniversary of the birth of Louise Brown, we know that Steptoe and Edwards were successful. The question than is, what did they know and what do we know now that they did not know? Edwards continued his career looking at preimplantation embryos and stem cells; but this work was so controversial he eventually abandoned it. He published a book

"Preconception and Preimplantation Diagnosis of the Human Genetic Disease" based on this work. Edwards was an extremely insightful person, so it is difficult to know what he knew and/ or predicted, but we can look at a few developments that have occurred that perhaps he did not envision. The work of Shinya Yamanaka's work with human Pluripotential stem cells in 2007 was predicted by Edwards, which resulted in Yamanaka's 2012 Nobel Prize. Edwards worked diligently at maturing immature eggs, yet this has not been realized today; Edwards understood its potential. Edwards was a verbal critic of high estrogen levels interfering with implantation. This has been proven to be a correct. The concept of freeze-all and understanding hyperstimulation syndrome is not apparent in his writing. Early on, he was an expert on pre-implantation diagnosis and embryo quality, primarily based on anatomical appearance. Yet, it is clear from his work that he anticipated markers, less crude for embryo quality. He was a proponent for single-embryo transfers. Endometrial receptivity was a mystery to Edwards and continues to be today. Did he envision the success of Fertility Preservation? Did he think there was potential for gamete rejuvenation? Certainly, religious questions, the registry and ethical issues remain unchanged. The question we must ask ourselves is what did Edwards not envision that we do today? And what do we not understand that will be clear to future generations.

IMMUNOLOGY OF PREGNANCY: WHAT SHOULD WE KNOW?

Anke Diemert, Germany

During the period of mammalian pregnancy two histoincompatible individuals, since the fetus not only inherits not only maternal, but also paternal antigens. Since fetal antigens are foreign to the maternal immune system, a tailored adaptation of the maternal immune system must be mounted to suppress the rejection of the semi-allogenic fetal tissue and to ensure pregnancy maintains until term. Important insights into how this tailored adaptation of the maternal immune system is operational have arisen from the last five decades of research in the area of reproductive immunology. Besides promoting a successful pregnancy outcome, this adaptation of the maternal immune and endocrine system during pregnancy can have significant health advantages as well as disadvantages for the mother and the offspring. It may improve maternal autoimmune disease activity, as seen in multiple sclerosis (MS), but enhances severity of viral infections, such as influenza. This observation highlights that the tailored adaptation of the maternal immune system affects organ-specific immunity at sites other than the uterus. Thus a better understanding of how the maternal adaptation to pregnancy is operational may aid the discovery of new therapeutic targets. Furthermore, maternal immune adaptation to pregnancy can be challenged. Prenatal challenges to which women particularly in Western societies are nowadays frequently subjected include high levels of stress perception, prescription-free self-medication and an unhealthy diet. It is still unknown how an altered maternal adaptation to pregnancy can be identified in the mother and current medical practice falls short to do so. If adequately mounted, the feto-maternal immune cross talk strongly supports placental function and fetal development. But if challenged, there is increasing evidence that it may subsequently result in poor fetal development. The poor fetal development observed in response to these frequently occurring and omnipresent prenatal challenges can result in health disadvantages for children later in life. The effect of such challenges on the fetal immune system is still only marginally understood and largely subclinical at time of birth. But an impaired children's health in response to prenatal challenges may occur despite an otherwise normal pregnancy outcome and birthweight. The immune system largely develops during fetal life and several central milestones of immune ontogeny are achieved



during fetal life and completed at birth. Taken together, the maternal immune adaptation occurring during pregnancy is of paramount importance and yields to more than a successful pregnancy outcome. It's delicate balance can result in advantages and disadvantages not only for maternal health, but also for fetal development and subsequent children's health.

EDWARDS AND STEPTOE RESEARCH FUND - RBMS LECTURE: THE BIRTH OF THE FIRST "TEST TUBE BABY" IN THE BRITISH PRESS

Katharine Dow

Reproductive Sociology Research Group (ReproSoc), University of Cambridge, UK

This lecture will present findings from an interdisciplinary research project examining how the British press represented IVF during the pivotal year of 1978. It will focus particularly on how national newspapers depicted the birth of Louise Brown, the world's first 'test-tube baby', at this time, with particular reference to the major protagonists of the story: Robert Edwards, Patrick Steptoe and the Brown family. The study entailed in-depth qualitative analysis of all the national newspapers' coverage of the story during 1978, supplemented with close reading of three memoirs: *A Matter of Life* by Steptoe and Edwards, *Our Miracle Called Louise* by John and Lesley Brown and *My Life as the World's First Test-Tube Baby* by Louise Brown. The lecture will discuss key examples from this body of research with reference to the historical context of the late 1970s in Britain, a time of political and economic crisis and resurgent social conservatism. Media representations of IVF are a familiar, yet under-studied, part of the technology's history. IVF has long featured in media stories and assisted reproductive technologies seem to hold a particular fascination for journalists compared to many other medical treatments and techniques. IVF, like other assisted reproductive technologies, is also familiar to most people, including potential patients, through its portrayal in the media. In the year of Louise Brown's fortieth birthday, this lecture will reflect on the importance of how this story was framed at the time and how this helped normalise the technology. Although, as attendees of this congress will know, IVF was a controversial technique throughout its development, by 1978, the British press had come to represent the birth of Louise Brown as both a success and a source of hope. They did so in large part through sympathetic portrayals of the main protagonists. During 1978, a remarkably consistent positive story emerged across tabloid and broadsheet newspapers in which the main pairs of protagonists, Steptoe and Edwards and Lesley and John Brown, came to be metonymic of British science and infertile couples respectively. In the dominant 'success' narrative of the birth of Louise Brown as depicted in the British press in 1978, Edwards and Steptoe seemed to embody 'British' values of industriousness, perseverance, altruism, ingenuity and teamwork. Thus, their success was simultaneously a British one. Lesley and John Brown came to stand as 'ordinary' people who were benefiting from science to achieve the normal goal of having a child who was biogenetically related to both of them; Louise Brown herself was portrayed as a blonde, blue-eyed 'perfect' baby. This created a dominant narrative in which IVF was, contrary to the more vivid imaginings of science fiction authors or religious authorities, simply a means of helping married heterosexual couples have babies. With Louise Brown's birth as its origin story, IVF thereby came to stand for the potential happiness of infertile people and a bright future for British science and industry.

COUNTERCURRENT 40 YEARS ON: MOVING TOWARDS STRATIFYING PATIENT TREATMENT AND REMOVING SUBJECTIVITY FROM IVF PRACTICE

Simon Fishel

CARE Fertility Group, UK

25th July 1978 was the birth of the first IVF baby and, despite the residual disbelief, ethical concerns and social antagonism it heralded a new era for the treatment of childlessness. This unique event was the culmination of decades of scientific effort and moral debate about the potential for IVF¹. Although doubts remained, believers from the medical science community, rational elements of society and the pioneering patients were prescient in the value it would have on individual human health and social wellbeing in general – from aiding countries with declining birth rates, improving national health economics with regard to the passage of monogenic disease and redefining family life. And although much of the modern technology of IVF and its impact on society is still to be advanced, the innovation in practice at the clinic level, particularly in terms of embryology and genetics has revolutionised success rates. However, we are fast learning that a generalised approach to medical treatment can be materially improved upon by diminishing subjectivity and improving our awareness of distinctiveness in an individual. The former can be helped by technology, both in hardware and software systems and the use of AI; whilst advanced genetics is abetting an individualised approach to patient therapy. We shall discuss inchoative examples of this and opportunities for future strategies.

1. Fishel, S. First in vitro fertilization baby—this is how it happened. 2018, *Fertility and Sterility*;110:5–11.

LASER USE IN GENITOURINARY SYNDROME OF MENOPAUSE

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Objective: The aim of this study was to evaluate the long-term efficacy and safety of Vaginal Erbium Laser (VEL) for the treatment of genitourinary syndrome of menopause (GSM) and stress urinary incontinence (SUI) **Methods:** The study was performed on an outpatient basis using an erbium laser (XS Fotona Smooth™, Fotona, Ljubljana, Slovenia) in postmenopausal women (PMW, n= 205) treated with 3 laser applications every 30 days. Symptoms were assessed before and after 1, 3, 6, 12, 18 and 24 months, using the visual analog scale (VAS) and the vaginal health index score (VHIS). In addition, SUI was evaluated with the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF). **Results:** VEL treatment significantly improved VHIS, as well as vaginal dryness and dyspareunia scores (p<0.01) up to the 12 months after the last VEL treatment, while the values were similar to the baseline after 18 and 24 months. In 114 PMW suffering from mild-moderate SUI, VEL treatment significantly (p<0.01) improved ICIQ-SF score, up to the 12 month of observation. VEL was well tolerated with less than 3% of patients discontinuing treatment due to adverse events. During our observation period, 174 (84.9 %) PMW asked to repeat VEL procedure for GSM, and 96 patients (69.6%) for the treatment of SUI. **Conclusions:** Present results suggest that VEL is effective, safe and well accepted for the treatment of GSM and SUI. The major concern is that our large longitudinal study is not controlled by a placebo (sham procedure) group. However, the Italian National Health Care System and the vast majority of Insurance Companies do not cover VEL at the moment, and that the patient must pay on his own. Arguably, the out-of-pocket expenses may compel the patients to avoid the repetition of a potentially ineffective procedure. The high percentage of patients repeating the procedure can be taken as an indirect evidence of the efficacy of VEL.



UTEROTONIC AGENTS FOR PREVENTING POSTPARTUM HAEMORRHAGE: A NETWORK META-ANALYSIS

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Background: Postpartum haemorrhage (PPH) is the leading cause of maternal mortality worldwide. Prophylactic uterotonic drugs can prevent PPH, and are routinely recommended. There are several uterotonic drugs for preventing PPH but it is still debatable which drug is best. **Objectives:** To identify the most effective uterotonic drug(s) to prevent PPH, and generate a ranking according to their effectiveness and side-effect profile.

Search methods: We searched Cochrane Pregnancy and Childbirth's Trials Register (1 June 2015), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) for unpublished trial reports (30 June 2015) and reference lists of retrieved studies.

Selection criteria: All randomised controlled comparisons or cluster trials of effectiveness or side-effects of uterotonic drugs for preventing PPH. Quasi-randomised trials and cross-over trials are not eligible for inclusion in this review. **Data collection and analysis:** At least three review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. We estimated the relative effects and rankings for preventing PPH \geq 500 mL and PPH \geq 1000 mL as primary outcomes. We performed pairwise meta-analyses and network meta-analysis to determine the relative effects and rankings of all available drugs. We stratified our primary outcomes according to mode of birth, prior risk of PPH, healthcare setting, dosage, regimen and route of drug administration, to detect subgroup effects. The absolute risks in the oxytocin are based on meta-analyses of proportions from the studies included in this review and the risks in the intervention groups were based on the assumed risk in the oxytocin group and the relative effects of the interventions. **Main results:** This network meta-analysis included 140 randomised trials with data from 88,947 women. There are two large ongoing studies. The trials were mostly carried out in hospital settings and recruited women who were predominantly more than 37 weeks of gestation having a vaginal birth. The majority of trials were assessed to have uncertain risk of bias due to poor reporting of study design. This primarily impacted on our confidence in comparisons involving carbetocin trials more than other uterotonics. The three most effective drugs for prevention of PPH \geq 500 mL were ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination. These three options were more effective at preventing PPH \geq 500mL compared with oxytocin, the drug currently recommended by the WHO (ergometrine plus oxytocin risk ratio (RR) 0.69 (95% confidence interval (CI) 0.57 to 0.83), moderate-quality evidence; carbetocin RR 0.72 (95% CI 0.52 to 1.00), very low-quality

evidence; misoprostol plus oxytocin RR 0.73 (95%CI 0.60 to 0.90), moderate-quality evidence). Based on these results, about 10.5% women given oxytocin would experience a PPH of \geq 500 mL compared with 7.2% given ergometrine plus oxytocin combination, 7.6% given carbetocin, and 7.7% given misoprostol plus oxytocin. Oxytocin was ranked fourth with close to 0% cumulative probability of being ranked in the top three for PPH \geq 500 mL. The outcomes and rankings for the outcome of PPH \geq 1000 mL were similar to those of PPH \geq 500 mL, with the evidence for ergometrine plus oxytocin combination being more effective than oxytocin (RR 0.77 (95% CI 0.61 to 0.95), high-quality evidence) being more certain than that for carbetocin (RR 0.70 (95% CI 0.38 to 1.28), low-quality evidence), or misoprostol plus oxytocin combination (RR 0.90 (95% CI 0.72 to 1.14), moderate-quality evidence). There were no meaningful differences between all drugs for maternal deaths or severe morbidity as these outcomes were so rare in the included randomised trials. Two combination regimens had the poorest rankings for side-effects. Specifically, the ergometrine plus oxytocin combination had the higher risk for vomiting (RR 3.10 (95% CI 2.11 to 4.56), high-quality evidence; 1.9% versus 0.6%) and hypertension [RR 1.77 (95% CI 0.55 to 5.66), low-quality evidence; 1.2% versus 0.7%], while the misoprostol plus oxytocin combination had the higher risk for fever (RR 3.18 (95% CI 2.22 to 4.55), moderate-quality evidence; 11.4% versus 3.6%) when compared with oxytocin. Carbetocin had similar risk for side-effects compared with oxytocin although the quality evidence was very low for vomiting and for fever and was low for hypertension. **Authors' conclusions:** Ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination were more effective for preventing PPH \geq 500 mL than the current standard oxytocin. Ergometrine plus oxytocin combination was more effective for preventing PPH \geq 1000 mL than oxytocin. Misoprostol plus oxytocin combination evidence is less consistent and may relate to different routes and doses of misoprostol used in the studies. Carbetocin had the most favourable side-effect profile amongst the top three options; however, most carbetocin trials were small and at high risk of bias. Amongst the 11 ongoing studies listed in this review there are two key studies that will inform a future update of this review. The first is a WHO-led multi-centre study comparing the effectiveness of a room temperature stable carbetocin versus oxytocin (administered intramuscularly) for preventing PPH in women having a vaginal birth. The trial includes around 30,000 women from 10 countries. The other is a UK-based trial recruiting more than 6000 women to a three-arm trial comparing carbetocin, oxytocin and ergometrine plus oxytocin combination. Both trials are expected to report in 2018. Consultation with our consumer group demonstrated the need for more research into PPH outcomes identified as priorities for women and their families, such as women's views regarding the drugs used, clinical signs of excessive blood loss, neonatal unit admissions and breastfeeding at discharge. To date, trials have rarely investigated these outcomes. Consumers also considered the side-effects of Consultation with our consumer group demonstrated the need for more research into PPH outcomes identified as priorities for women and their families, such as women's views regarding the drugs used, clinical signs of excessive blood loss, neonatal unit admissions and breastfeeding at discharge. To date, trials have rarely investigated these outcomes. Consumers also considered the side-effects of uterotonic drugs to be important but these were often not reported. A forthcoming set of core outcomes relating to PPH will identify outcomes to prioritise in trial reporting and will inform futures updates of this review. We urge all trialists to consider measuring these outcomes for each drug in all future randomised trials. Lastly, future evidence synthesis research could compare the effects of different dosages and routes of administration for the most effective drugs.



DEBATE: SOCIAL FREEZING: WHAT ARE THE RESULTS OF OOCYTE SURVIVAL, PREGNANCY RATE AND OBSTETRICS OUTCOME?

Norbert Gleicher

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Cryopreservation of oocytes to expand a woman's reproductive lifespan, has been rapidly increasing in popularity. Though in principle an attractive concept, its presentation to the public has, at times, been seriously flawed in that limitations of oocyte freezing either have not been presented or are seriously distorted. In that, the preservation of oocytes has become part of what we have called the "industrialization" of assisted reproductive technology (ART), where in vitro fertilization (IVF) and related procedures are no longer viewed a primarily highly complex clinical treatments but product lines to be sold to a gullible public. It, therefore, should not surprise that oocyte cryopreservation, at least in the U.S., is promoted in "egg-freezing parties" and is widely misrepresented to the public as no longer experimental (the ASRM only exempted egg freezing for women at imminent threat of losing ovarian function due to iatrogenic interventions since risk-benefit considerations in those situations, of course, differ). It should also not surprise that Wall Street money has entered the fray and, in view how radically women are now delaying childbirth in the U.S., considers this treatment a "growth industry" (U.S. national birth rates were just reported to have fallen to the lowest rates since WWII). Mostly driven by investor money, IVF centers have been established that do nothing else but oocyte cryopreservation to expand women's reproductive lifespans. One must wonder how such centers maintain their overall IVF competence? One company, founded with a \$200 million investment budget, is built on a business model that expects all young women and men to preserve their gametes at young ages via cryopreservation. The model further assumes that all will later in life prefer IVF pregnancies that allow prior testing of their (from young oocytes and semen produced) "young" embryos for chromosomal abnormalities with preimplantation genetic testing for aneuploidy (PGT-A) and, therefore, practically become lifelong clients of the company, starting with cryopreservation of gametes, later thawing of gametes and subsequent IVF cycles with PGT-A. Remarkably, these projects are marketed to the public with significant financial muscle, even though, oocyte cryopreservation for these purposes, rightly, is still considered an experimental procedure since nobody can accurately advise women at different ages what pregnancy and live birth chances down the road cryopreservation of x or y numbers of eggs will really offer. Similarly, any clinical efficacy of PGT-A was just recently, for the second time in 10 years, again rejected by Practice Committees of ASRM and SART. But once ART enters "industrialization," scientific truth no longer matters. The only truth that does matter is financial profit.

ADVANCED MATERNAL AGE: UNTIL WHAT AGE AUTOLOGOUS AND UNTIL WHEN HOMOLOGOUS EGGS? THE REPRODUCTIVE ENDOCRINOLOGIST'S POINT OF VIEW

Norbert Gleicher

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In the U.S., women above age 40 are the only age group in which the number of pregnancies has been increasing. The reasons are multifactorial and more complex than generally described in the

literature. It is correct that conscious delays of conception play a major role, and that many of these delays are the consequence of career choices. But recent studies also demonstrated that inability to find the "right" partner also plays a major role. As a consequence, infertility centers, especially in economically developed countries, treat increasing numbers of older women and mean-ages of patients are steadily increasing. Our center is at the forefront of these developments with for the first time exceeding a median-age of 43.0 years in 2017. This makes our center's patient population by far the oldest of any reporting IVF center in the U.S. and, likely, in the world. We, therefore, have for many years been facing the question, which age (if any) is too old to still pursue IVF pregnancies with autologous eggs? Our answer to this question has evolved, as our capabilities in treating older women have improved. Our basic opinions on this subject have, however, not changed and can be summarized as, "*we do not feel qualified to tell our patients how to live their lives.*" What we mean by this is that: (i) We do not believe in artificial age cut offs since there are young women with very "old" ovaries and older women with surprisingly "young" ones. There are also young women who are too medically labile to go through pregnancy and there are older women who physically are in perfect shape to experience the stress pregnancy exerts on all body parts. Who qualifies for IVF and who does not, therefore, at our center is never solely based on female age. (ii) We also feel incapable of guessing what represents a positive risk/benefit and/or cost/benefit situation for a given patient. Some patients consider a 5% pregnancy chance as tremendous, while others feel that a 20% chance is too low. We, therefore, will never advise patients that they "must" pursue a certain treatment (i.e., for example egg donation) and would, otherwise, receive no treatment at our center. Egg donation, of course, in practically all women above age 40 and in many women with premature ovarian aging even at younger ages offers superior pregnancy chances to use of autologous eggs. But for many women that is not the only criteria, and the number of women for whom egg donation does not offer an (immediate) option is considerable. We in this talk will demonstrate how women of even very advanced ages in many cases can still be given reasonable pregnancy and live birth chances.

SPECIAL COGI COUNTERCURRENT LECTURE: IVF OUTCOMES OVER THE YEARS. IS THE LIVE BIRTH RATE (LBR) RISING OR DECLINING, AND WHY?

Norbert Gleicher

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We in this lecture will present worldwide IVF live birth data for the last decade of available data. Though most of these data were obtained from publicly accessible data sets, they have never before been presented over such a longitudinal time period and associated with introduction of certain new practice patterns to in vitro fertilization (IVF). We can state with considerable certainty that the presented data will surprise. There are a variety of reasons for that but, likely the biggest surprise is that IVF outcomes, widely assumed to have been constantly improving, actually, for quite some time have failed to do. Though different regions in the world, interestingly, have quite steadily maintained outcome differences, live birth rates all over the world have, almost uniformly, declines, with 2014 rates often falling below 2002-2004 rates. These parallel declines in greatly varying patient populations strongly imply responsibility for worldwide practice changes in IVF. Though this in itself is a remarkable finding, even more interesting are observed negative associations with specific practice changes. Those are particularly pronounced with introduction of uniform blastocyst-stage embryo culture and single



embryo transfer, embryo banking, preimplantation genetic testing for aneuploidy (PGT-A) and or some other unproven and/or unvalidated add-ons to IVF over the last decade. Though associations do not automatically reflect causations, their coordinated timing in highly variable populations all over the world strongly supports causation. It appears that these new add ons to IVF are especially harmful in poorer prognosis patient who produce only small egg/embryo numbers. In those patients, embryo selection methods are especially harmful. The unnecessary loss of every embryo counts in poor prognosis patients more than in good prognosis patients with excellent embryos in large numbers. This is especially true with first fresh cycle outcome analyses rather than cumulative pregnancy chances from a complete embryo cohort produced in a single IVF cycle. Many of these “unproductive” add-ons to IVF have in the last decade been introduced into clinical practice based on false premises, often claims of efficacy using inappropriate statistical models, based on totally untested and/or unvalidated hypotheses and, at times, even based on blatant misrepresentations in commercially motivated marketing campaigns. The cumulative result are declines in live birth rates all over the world, interrupting 30 years of steadily improving IVF outcomes. We will also offer evidence that these negative developments in IVF also appear connected to what we have come to call the “industrialization and “commoditization” of IVF around the world. The former term is defined by increasing replacement of physician-owned IVF practices by investor-owned practice chains, resulting in a switch in competitive parameters between IVF centers from cycle outcomes to revenue and profit (i.e., “commoditization”) by marketing add-ons to routine IVF practice to increase revenue. Not surprisingly, these developments are also associated with declining patient satisfaction.

FAMILIES CREATED BY IDENTITY-RELEASE EGG DONATION

Susan Golombok

University of Cambridge Centre for Family Research, UK

Research on children born through egg donation has focused entirely on children with anonymous egg donors. However, since the removal of donor anonymity in the UK in 2005, all egg donors have been identifiable. Therefore, children who are aware of their donor conception are likely to grow up knowing that they may discover the identity of their egg donor on reaching age 18. Whereas this may be viewed as beneficial in that they will be able to find out about their genetic origins should they so wish, it is not known how the prospect of meeting the egg donor later in life affects the nature and quality of family relationships in childhood. It has been suggested that identity-release donation may negatively influence family functioning as the donor may be perceived as an ongoing presence within the family, or as posing a threat to the mother-child relationship. This may affect mothers' thoughts and feelings about their parental role, particularly their sense of entitlement and confidence as a mother. Findings will be presented from the first study worldwide to investigate children born using identifiable egg donors. Eighty-five families created using identifiable egg donors and a comparison group of 65 families created through IVF using their own gametes, all with a child aged 6-18 months, were recruited through eight fertility clinics in the United Kingdom. The quality of the parent-infant relationship was assessed for mothers and fathers separately using (i) a standardised interview designed to assess parents' representations of their relationship with their child with variables such as *expression of anger towards the child, joy/pleasure in the child, parental confidence, disappointment in parenthood, warmth towards child, hostility towards child, child affection, child anger, child controlling/manipulating, and child rejecting*; and (ii) an observational assessment of parent-infant interaction involving a

free play task that produced variables such as *parental sensitivity to child, parental hostility to child, child's responsiveness to parent, and child's involvement of parent in the interaction*. In addition, a qualitative analysis was conducted of the mothers' feelings about having a genetically unrelated child. The assessment of the quality of the parent-child relationship at the representational level showed very few differences between egg donation and IVF families. Differences were found between egg donation and IVF families in the observational assessment of parent-child interaction, but only between mothers and their children, and only when data from twin families were included. Mothers in both family types had representations of the mother-child relationship in which they viewed themselves as high in warmth and joy, moderate to high in child-focus and competence, and low in disappointment and anger. Egg donation and IVF mothers both represented their children as affectionate and happy, with low levels of anger, rejecting or controlling behaviours. Similarly, egg donation and IVF fathers had representations of themselves that were moderate to high in warmth, joy and confidence, and low in disappointment and anger, with representations of the child as affectionate and happy and neither rejecting nor controlling. Thus, parents' representations of the parent-child relationship indicated a high quality of relationship in both family types. With regard to parent-child interaction, egg donation mothers were less sensitive than IVF mothers, and egg donation children were less emotionally responsive and involving of the mother than were IVF children, indicating a poorer quality of mother-child interaction among the egg donation families. When data from families with twins were omitted, no differences were found between egg donation and IVF mother-child dyads, suggesting that being the parent of twins may have proved more challenging for egg donation mothers. Nevertheless, the mean scores of both family types on all variables were at the upper end of the scales, indicating good relationship quality. Mothers in both groups showed particularly low hostility towards their children (i.e. no signs of boredom or discontent), which has been found to be a feature of parent-child interactions where parents have wanted to have children for a long time. That egg donation families are functioning well when their children are aged 6-18 months old, and have more similarities than differences to IVF families, should prove reassuring to clinicians, prospective egg donation parents, and families already created in this way. The qualitative analysis showed that many mothers were concerned during pregnancy about how they would feel about having a genetically unrelated baby. Following the birth, there was variation in mothers' feelings toward their infants. Most bonded immediately, but for others, bonding developed over time. Despite their concerns, all of the mothers felt that the baby was their 'own child' by the end of the first year.

RESEARCH ON ART FAMILIES: AN HISTORICAL PERSPECTIVE

Susan Golombok

University of Cambridge Centre for Family Research, UK

This presentation will describe the findings of research on the quality of parent-child relationships and the psychological adjustment of children in ART families from the late-1980s to the present day. The European Study of Assisted Reproduction Families was initiated in 1992, and followed up IVF families and donor insemination families, in comparison with matched groups of adoptive and natural conception families, in Spain, Italy, the Netherlands and the United Kingdom. In-depth assessments of the families were carried out when the children were aged 6 years, 12 years and, in the United Kingdom only, at 18 years. The ART families were found to be functioning well. However, not one set of the 111 donor insemination parents in the study had told their 6-year-old children about the method of their conception, and less



than 10% had disclosed this information by age 12. In order to investigate the impact of disclosure on family functioning, a new longitudinal study was initiated in the United Kingdom at the millennium. Families formed through egg donation, donor insemination and surrogacy, and a matched comparison group of natural conception families, were followed up when the children were aged 1, 2, 3, 7, 10 and 14 years. The findings replicated the positive outcomes found in the earlier European study. A higher proportion of parents in the more recent study had told their children about their genetic origins but many had not disclosed this information. Among the disclosing families, the children who had been told about their origins in their preschool years had more positive relationships with their parents at adolescence. In addition to these studies of traditional families created through ARTs, findings will be presented from studies of parenting and child development in non-traditional families created by donor insemination and surrogacy, including families headed by lesbian mothers, gay fathers and single mothers by choice, which similarly point to well-functioning families in terms of parenting and child development. Research on the outcomes of ART for parents and children is not only of interest in its own right, but also increases understanding of the relative importance of family structure and family relationships for children's psychological well-being. Taking all of the findings together, it appears that the quality of family relationships and the wider social environment are more influential in children's psychological development than are the number, gender, sexual orientation or biological relatedness of their parents or the method of their conception. The presentation will be based on Susan Golombok's 2015 book, *Modern Families: Parents and children in new family forms*.

MOSAICISM IS NOT AN OBSTACLE FOR PGS TO WORK

Tony Gordon, UK, Santiago Munné, USA

Chromosomal Mosaicism, the presence of several cell lines with different chromosome content, was described decades ago when FISH was used for PGT. With the switch to blastocyst biopsy and the advent of comprehensive molecular techniques such as qPCR and aCGH, the DNA of several biopsied cells was analyzed together precluding the detection of mosaicism. Next Generation Sequencing, which has higher resolution than previous PGT techniques allows again for the detection of mixed samples, detecting in a 10 cell biopsy differences from 20-80% normal to abnormal ratios of cells. This has changed the binary classification of embryos (normal or abnormal) into a gradient in which embryos can be classified into euploid (normal), mosaic (and a gradient of high to low) and fully aneuploid. Several articles have described that NGS-classified mosaic embryos implant less and miscarry more than euploid ones, but some make into babies. Within these mosaics, those with chaotic mosaicism (involving 3 or more chromosomes on mosaic form) seldom implant, those with >40% abnormal cells have 20-30% ongoing pregnancy potential, and those that have 20-40% abnormal cells have ongoing pregnancy rates of about 50%, compared to 60-70% for NGS-classified euploid embryos. This is probably due to better survival potential and faster cleavage rate of the euploid cell line than the aneuploid cell line, but a critical mass of euploid cells is needed. This interpretation is supported by a mouse model (Bolton et al. 2016) in which chimeric embryos were made by combining different ratios of normal to abnormal cells, and in which embryos survived to term and formed completely normal pups the more euploid cells they had. So far, babies born from the transfer of human mosaic embryos have also been all chromosomally normal, although more data to proof safety is needed since only 0.2% of pregnancies in vivo are mosaic and affect the fetus. Preliminary evidence suggests that replacing NGS-classified euploid embryos provides higher ongoing pregnancy rates than replacing aCGH-classified embryos. As a screening technique, the

screening technique to select the embryos with the best potential, being able to detect mosaicism is an advantage. However, cumulative pregnancy rates might be affected if mosaics are never replaced. As such the recommendation is to first transfer euploid-classified embryos, followed by low grade mosaics, followed by high grade mosaics.

Although some had argued that some pregnancies might be obtained from replacing aneuploid embryos, their observations were based on aCGH data, which was unable to detect most mosaics, and probably those embryos were mosaics. Indeed, positive predictive values for qPCR and other earlier techniques were 96%. However, now that we can identify mosaics, those aneuploid embryos probably have a higher positive predictive value closer to 100%. The risk of miscarriage for such embryos is huge. In summary, mosaicism detection is a blessing to PGT by reducing the error rate of euploid and aneuploid classified embryos. For those classified as mosaic, the recommendations from COGEN, and PGDIS and several articles are to deprioritize their transfer but do not discard them.

PGT FOR ALL PATIENTS 35 AND OLDER

Tony Gordon, UK, Santiago Munné, USA

It is unquestionable that chromosome abnormalities are the main cause of embryo loss with advancing maternal age. Aneuploidy and other abnormalities increase from 40% in in-vitro conceived human embryos of young women, to 60% in women 35-37, to 80% in women 41 and older. The replacement of fully aneuploid embryos seldom results in ongoing pregnancies. The exception is when mosaic embryos are replaced (knowingly or undetected), but embryos that are completely abnormal seldom reach term. Indeed, using PGT v2 techniques, when euploid embryos are replaced, they implant equally well at any age, demonstrating that the decrease in implantation potential with maternal age mostly results from aneuploidy. PGT v2 as currently applied consist on performing blastocyst biopsy and analyzing 5-10 cells from the TE using comprehensive molecular techniques. The error rate reported by several labs using different techniques ranges between 0% to 4%. There is only one study comparing the effect of cleavage-stage and blastocyst biopsy on implantation, and it shows no detrimental effect for the second and significant damage from the first (Scott et al. 2012), suggesting that the biopsy was responsible for the lack of clinical success of the earlier PGT v1, which then involved FISH analysis and cleavage-stage biopsy. So far there have been five Randomized Clinical Trials (RCTs) using PGT v2, all showing an improvement in clinical results. Some of these studies have been criticized for being small, although showing statistical significance, or single-center, thus applying only to fertility centers with significant skills. One study however, the STAR study, is a "real-world" multi-center (35 centers), multi PGT lab study (9 Labs). Its results showed that PGT improved ongoing pregnancy rates per transfer in women 35 and older, while it made no difference in women younger than 35. These results also coincide with the SART 2015 data, a repository of most USA cycles, in which again PGT improved results for women 35 and older but not in young ones. These two studies represent an average of clinics, not the best and most experienced clinics. Since there is 30-40% aneuploidy in embryos of young patients, is puzzling that there is no beneficial effect, unless the biopsy itself is again eliminating screening potential. There are several studies showing that biopsing more than 10 cells decreases implantation potential, and the blastocyst biopsy technique has not been standardized. Until then, it is probably recommendable that only centers with high expertise in blastocyst biopsy should apply it to younger patients.

NIPT IN THE CONTEXT OF IVF AND PGS

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Cell-free DNA (cfDNA) testing (also known as non-invasive prenatal testing/screening, NIPT/S) is a well-established technology for the evaluation of risk for fetal trisomies 21,18 and 13. Sensitivity and specificity of cfDNA testing is superior, both in terms of higher DR and substantially lower FPR, to that of all other methods combining maternal age, first- or second-trimester ultrasound findings and first- or second-trimester serum biochemical analysis (Gil et al, *Ultrasound Obstet Gynecol* 2017). CfDNA testing on IVF (singleton and twin) pregnancies present some pitfalls and limitations. Preliminary reports of cfDNA testing performances in twins show sensitivity and specificity for T21 similar to singletons (Gil et al, *Ultrasound Obstet Gynecol* 2017; Liao et al, *Prenatal Diagn* 2017). Due to the paucity of cases, performances on for T13 and 18 cannot be established in twin pregnancies. In addition, IVF (twin and singleton) pregnancies show an increased risk of no test result due to low amount of cell free fetal circulating DNA fraction (fetal fraction) and/or insufficient quality metrics (Sarno et al, *Ultrasound Obstet Gynecol* 2016). However, a relevant role for determining test accuracy and no result rate, particularly in dizygotic twin pregnancies, relies on the applied method fetal fraction measurement which may vary depending on testing technology (Struble et al, *Fetal Diagn Ther* 2014; Sarno et al, *Ultrasound Obstet Gynecol* 2016). Finally, the rate of singletons who are results of a vanished twin in IVF pregnancies is ~20% (Chauhan et al, *Am J Obstet Gynecol* 2010). Therefore, as cfDNA test analyses circulating fragments derived from apoptotic placental cytotrophoblasts, an increased rate of false positive results and fetal sex discordances should be expected in vanishing twin pregnancies due to the persistence of the circulating DNA fragments derived from the reabsorbed fetus (Curnow et al, *Am J Obstet Gynecol* 2015; Thurik et al, *Prenat Diagn* 2015). In the context of IVF pregnancies, there might be some that underwent preimplantation genetic testing for aneuploidies (or PGT-A, previously known as PGS) on trophoctodermic cells (TE) prior to embryo transfer. Depending on the type of applied PGT-A technology, a mosaic aneuploidy can be detected in up to 21% of the tested embryos (Greco et al., 2015; Munné and Wells, 2017). It is obvious that euploid embryos should be privileged over mosaic embryos for transfer, however sometimes only mosaic embryos are available. However, although mosaic embryo transfer is associated with poorer outcomes when compared with the euploid control embryos, there is a compelling concern that viable embryos may be unjustifiably discarded due to concerns over mosaicism. In fact, the cytogenetic experience conducted on first trimester prenatal diagnosis on placental cytotrophoblast (the placental tissue derived from the embryonic trophoctoderm) shows that only ~11% of cases with mosaic cytotrophoblast are true fetal mosaicisms and that the likelihood that a mosaic trisomy in cytotrophoblast is confirmed in amniocytes largely depends on the distribution of the abnormal cell line in the two placental layers (cytotrophoblast and mesenchyme) and on the type of chromosome involved in the mosaic aneuploidy (Grati et al, *RBMO* 2018). Results obtained from PGT-A are therefore essential information for decision-making process and management of prenatal genetic testing of pregnancies obtained after mosaic aneuploidy embryo transfer. During the talk, the following topics will be presented and discussed:

- Overview of cfDNA testing performances in twin and IVF pregnancies;
- Pitfalls of cfDNA testing in vanishing twins;
- Fetal fraction measurement and internal quality metrics with cfDNA testing technologies;

- Management, in terms of prenatal testing, of pregnancies achieved after aneuploid mosaic embryo transfer detected by PGT-A/PGS;
- Clinical utility of cfDNA testing in pregnancies achieved after aneuploid mosaic embryo transfer.

SHOULD ANDROGENS BE ROUTINELY OFFERED TO OPTIMIZE QUALITY OF LIFE IN MENOPAUSE? - DEBATE

Alessandra Graziottin

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Androgens –testosterone and/or Dehydroepiandrosterone, DHEA - should be routinely offered to women after the menopause, with a few exceptions due to major contraindications (such as hormone-dependent cancers, at present). Well informed women should then made their own choice and give their written consensus to the androgen treatment, if interested.

Biologically speaking, sexual hormones, and androgens specifically, are women's best friend. At physiologic levels, in the fertile age, they maintain the glorious body at its best. After the menopause, the ovarian exhaustion causes a dramatic biological "asymmetry" in comparison to men. Women are deprived of the most powerful biological fuel for their brain, their health, their sexuality. Androgens (testosterone, DHEA, DHEA-Sulphate, androstenedione) work in interdependent synergy with estrogens (estradiol, estrone, estriol, and estetrol, in pregnancy) that deserve to be fully unveiled and explored. Indeed, in the life span after puberty women's health relies on estrogens and androgens. Three major facts, rooted in biological and clinical mistakes, have shadowed the role of androgens for women's health:

1. the use of different units to measure sexual hormones (picograms for estradiol, nanograms for testosterone, micrograms for DHEA and DHEA-S) has generated for decades the wrong idea that estradiol is quantitatively the most abundant sexual hormone in women. This idea, shared by physicians and lay people alike, has marginalized the role of androgens, particularly after the menopause, with a dramatic reduction both in quality of health and longevity in health for women;
2. when testosterone patches were investigated, they were studied just to prove that women's sexuality could be improved (in fact with a limited benefit, from 1 to 2 sexual encounter/month) with a total neglect of the many advantages testosterone could have offered to prevent/reduce the risk of cognitive impairment, Parkinson disease, sarcopenia, osteopenia/osteoporosis, to modulate/reduce the progression of autoimmune diseases, to improve the anemia of the elderly, the bladder function and the pelvic floor tonus (the bladder wall and the elevator ani are extremely rich of androgen receptors);
3. lack of long prospective clinical trials on systemic DHEA, and ideologically distorted analysis of a few small studies, have marginalized the huge health impact that is clinically evident when well-tailored androgens and estrogens treatments are carried out in the long term, in synergy with appropriate healthy lifestyles. (Vaginal prasterone (DHEA) seems to be very promising)

Women would have been most interested in testosterone therapy (with patches or other routes of administration), and with DHEA, at different dosages, had they known the many health-related systemic benefits they could have got in the long term, and that a smarter sexuality was just the flower in the buttonhole of a more rewarding longevity in health for the individual woman, besides the couple. The presentation will highlight:



- the key endocrinological characteristics of testosterone and DHEA, with focus on the concept of “intracrinology” for safety considerations
- reasons of the “androgen’s neglect” and “androgen’s dismiss”
- the many different biological benefits women can get for a more rewarding longevity in health
- the specific impact on sexuality, from the biological, psychosexual and relational point of view, both with systemic and vaginal treatments (including Prasterone (DHEA))
- the comprehensive reasons why a life-long androgen therapy (with DHEA and/or testosterone, either systemic or topical, with or without estrogens) may help women to age “in autonomy, dignity and grace” as the Author’s mother used to say, having enjoyed this treatment for more than 35 years, until the very last moments of her life.

40 years of Author’s clinical practice, using estrogens (and progesterone/progestins in women with intact uterus), testosterone and DHEA, with lifelong well-tailored individualized hormonal treatment, on thousand of patients, strongly support and endorse the Author’s considerations. Androgens should be routinely offered to every woman, with clear explanations of pros and cons, including the lack of “pro-androgens” guidelines in women and written consensus, with the goal of optimizing her health and quality of life -including couple’s sexuality, if welcomed-after the menopause and beyond.

A DESIGN FOR LIFE: HOW TO GET THE MOST OUT OF YOUR LABORATORY

Stephen J. Harbottle

Consultant Embryologist and Person Responsible; Cambridge IVF, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

The IVF laboratory represents the beating heart of any assisted conception service with its success or failure being dependant on the output of a series of routine and well established interlinked laboratory processes, resulting in the best possible quality human embryos for transfer or cryopreservation. The IVF laboratory and the technology deployed therein have evolved significantly since the pioneering work of Robert Edwards, Patrick Steptoe and Jean Purdy in the 1970s which culminated in the birth of the first test tube baby in 1978. Although the principles remain unchanged, the strategy, technology and methodology deployed within the IVF laboratory has evolved significantly in the last 40 years. In the modern IVF economy fertility treatment is rapidly becoming a business rather than a science. Competition to secure treatment activity is intensifying resulting in a realisation that obtaining average results is simply not good enough. The savvy IVF service manager will have already realised that to offer the best possible service to patients they not only need to ensure that their unit is as cost efficient and clinically effective as possible but also that they need to outperform their competition. This realisation, along with the ever-increasing demands of national and international regulations, guidelines and best practice documentation pertaining to laboratory and air quality standards, has prompted a paradigm shift in attitude. In addition, in a marketplace overflowing with techniques and devices promising performance enhancements, the concept of marginal gains has never been more relevant to our profession. In this presentation I lay down my personal tried and tested framework for best practice in the IVF laboratory. This ethos is underpinned by a robust laboratory design, consideration of the importance of air quality, a strategy for the detection and management of volatile organic compounds (VOCs) and a highly organised approach to process flow and laboratory efficiency. By way of examples, I detail my experiences of design, build and troubleshooting exercises over my 24 year career and the 5 design projects I have been involved in, managed

or overseen. I use my current unit, Cambridge IVF as a case study for what I believe to be a solid example of a robust and well-designed laboratory with respect to laboratory design, validation and quality. I will highlight the significant points for consideration including;

- The importance of good design before you commence a build project
- Keeping in control of the project during the build process
- Effective facility validation; from conception to commencing treatment
- Getting the best out of your existing IVF laboratory
- Do’s and don’ts
- The difference between process flow and personnel flow, how they complement one another and how they can be used to improve laboratory quality and efficiency
- The fine detail you should consider to make your lab stand out from your competition
- The importance of laboratory excellence in everything you do thereafter
- My mantra for IVF lab excellence; the critical importance of precision and accuracy.

The presentation is intended to be informative and interactive and should leave the audience with a clearer vision of how to get the best out of an existing laboratory or design the very best new laboratory possible.

FINDING A DONOR: TRUST THE CLINIC OR DO IT YOURSELF?

Joyce Harper

Embryology, IVF and Reproductive Genetics Group, Institute for Women’s Health, University College London, UK

A significant proportion of fertility treatment is ‘third-party reproduction’ – i.e. it involves the use of donor gametes or embryos. Sperm donation has been practised for decades as there is no need for a clinic to be involved. The digital era has opened up new ways of obtaining donor sperm. It is easy and comparatively cheap to access sperm online, for example, from one of the sperm banks that will ship sperm worldwide for home insemination. Additionally, a growing number of introduction websites offer women and couples the opportunity to meet a potential sperm donor online. Broadly three categories of women use introduction websites: those who want to have a child with no further involvement of the donor; those who wish to know the identity of the donor from the start and those who intend to electively co-parent, that is, to bring up the child together with the donor/father. Donors may choose to donate through introduction websites for altruistic reasons and/or in order to have greater involvement with the child. There are some donors who are motivated by the prospect of a sexual encounter, advertising their preference for natural insemination, via sexual intercourse or partial intercourse. Donor insemination treatment offered in licensed clinics protects the donor, recipient and offspring both medically and legally. Introduction websites are legal but unregulated, making it difficult to assess the scope and prevalence of the practice. Unlike donors and patients in licensed clinics, participants in these arrangements may not be made aware about the medical and legal implications of donor conception. When using donor sperm or eggs, it is key to be aware of the impact of genetic testing. There is a now a very real possibility that donor children can find half siblings, their donor or their donors relatives through ancestry genetic testing. The donor does not need submit their DNA to an ancestry database: if one of their relatives has, it may be possible for donor conceived adults to trace their donor. Donors and parents using this treatment must be made aware of this and we should encourage parents to tell their children of their genetic origin.

AN UPDATE ON REPRODUCTIVE GENETICS. WHAT DOES THE FUTURE HOLD?

Joyce Harper

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Since the structure of DNA was deciphered in 1953 by Watson, Crick and Franklin, we have come a long way. By 2001 we had sequenced the first human genome and James Watson had his genome sequenced in 2007 at a cost of \$1.5 million. Now it costs under \$1000 to sequence a human genome. Reproductive genetics consists of preconception testing, preimplantation genetic testing and prenatal diagnosis. For many decades, carrier screening has been used in high-risk populations, such as sickle cell for African populations. Now expanded carrier screening using panels for a number of mutations can be used for any couple wishing to have children. Data from the USA shows that 2% of couples found they were carrying a recessive mutation that they did not know about. Couples will require genetic counseling to discuss their reproductive options. They may wish to not have children, not have any testing, have prenatal or preimplantation genetic testing, use a gamete donor or adopt. New WHO nomenclature has stated that preimplantation genetic diagnosis (PGD) and screening (PGS) should be renamed preimplantation genetic testing for monogenic diseases (PGT-M), preimplantation genetic testing for chromosome structural rearrangements (PGT-SR) and preimplantation genetic testing for aneuploidy (PGT-A). For PGT, cells can be biopsied from the zygote, cleavage or blastocyst stage, but due to post zygotic mosaicism, most PGT is now done at the blastocyst stage. Instead of removing cells from the embryo, studies are ongoing to look at blastocoel fluid biopsy and using the spent culture media. The diagnostic techniques for PGT have changed greatly over the last 20 years, from using fluorescent in situ hybridisation through to next generation sequencing. The evolution has made the tests more efficient and enabled the detection of more genetic information. PGT-A is an IVF adjunct aimed at increasing the IVF live birth rate. For PGT-A, version 1 used mainly cleavage stage biopsy and fluorescent in situ hybridization but 11 randomized controlled trials (RCT) found that the procedure did not work. Five underpowered RCTs using PGT version 2 have shown benefits in both good and poor prognosis patients. The recently published ESHRE ESTEEM study shows that there were less transfers and less miscarriages in the PGT-A group but there was no difference in the live birth rate. Noninvasive prenatal testing (NIPT) uses sequencing to diagnose aneuploidy in the fetus and can also be used to detect some genetic abnormalities. Genome editing has become a hot topic as this could potentially be used for couples at risk of transmitting a genetic disease to their children. But first we need to ensure that the technique is safe and that society approves.

RECONSTRUCTED TISSUES FOR FEMALE FERTILITY TREATMENTS

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Introduction: Infertility is common after cancer due to surgical interventions or to radiation- or chemotherapy- impairment of the reproductive organs, including the uterus. Uterus-related infertility also exists for congenital reasons. Additionally, some women are advised not experience pregnancy due to partial uterine defect such as significant scarring in the uterine wall that may lead to uterine wall rupture during gestation or labour. After decades of animal studies, our group established the world's first successful human uterus transplantation as a fertility treatment for these patient groups and eight healthy babies have been born from a grafted uterus in our clinic. An additional four babies have now been born after the same fertility treatment at other centres

outside Sweden. Uterus-related infertility can thus be cured with uterus transplantation. However, the risky live-donor surgeries and the immunosuppression-related negative side effects cause concerns. We therefore investigate new potential alternatives that could avoid these hurdles by attempting to develop a personalized donor source using the patient's own cells and bioengineer uterine tissue suitable for as grafting material for fertility treatment. Our long-term goal is to develop a personalized whole-uterus construct that could replace the need for a live donor in a uterus transplantation setting and would not require immunosuppression following engraftment. However, our clinically relevant intermediate goal is to develop a bioengineered uterus tissue patch that may be used to reduce scar formation, improve healing and increase the uterine wall strength in situations where significant uterine impairment cause infertility. Our rodent studies showed that when mesenchymal stem cells and primary uterus cells were introduced to a decellularized uterus scaffold consisting of uterus-specific extra cellular matrix, this tissue restored fertility in a partial uterus injury model. Hence, a bioengineered uterus patch may become useful in a clinical situation to cover tissue defects caused for example by resection of placental tumours, extensive myomectomy or adenomyomectomy. Using the same rodent model, we are now attempting to improve the cellular reconstruction of the uterus scaffolds by introducing a temporary and local overexpression of VEGF that we believe could assist the graft construction and improve viability after engraftment of large bioengineered uterine tissue constructs. Furthermore, we have also begun translating our successful strategies to the sheep model to optimize our techniques further before tackling non-human primate models. **Methods:** Uterus scaffold generation via decellularization was performed on rat- and sheep uteri by perfusing detergents and ionic solutions through the vasculature of the whole organ. Detailed analysis on the extra cellular matrix (ECM) scaffold composition was established and recellularization was performed using species-dependent mesenchymal stem cells to evaluate the reconstruction efficiency. A local and temporary overexpression of VEGF in the rat cells was established by developing a tetracyclin-dependent CRISPR/dCas9 activation system. **Results:** We successfully removed all cells from whole rat- and sheep uterus while maintaining the extra cellular matrix structure and vascular conduits intact. These uterine tissue scaffolds provide us with a good building frame to add personalized cells and enable future engraftment with vascular anastomoses. We further assessed the morphological-, biological- and mechanical composition of the sheep scaffolds and successfully repopulated them with foetal mesenchymal stem cells to confirm scaffold biocompatibility. Our CRISPR/dCas9 modified rat cells increased the VEGF-expression 3-fold compared to non-modified cells and have the potential to provide regeneration support. **Discussion:** The uterus-specific extra cellular matrix structure together with the added cells may have a physical- and a biological 3D-structure that is advantageous for uterus repair. The potential beneficial in vivo effects from a temporary and local tetracyclin-dependent VEGF-overexpression from CRISPR/dCas9 modified rat cells remain to be investigated. The development of a whole-sheep uterus extra cellular matrix scaffold have provide us with a research platform to conduct whole uterus reconstruction- and transplantation studies of bioengineered uteri of similar size to a human uteri.

CAN ARTIFICIAL INTELLIGENCE HELP TO SELECT VIABLE EMBRYOS?

Christina Hickman, UK

Accurate and consistent selection of embryos for transfer, cryopreservation and discarding is critical for effective IVF treatment, whether to improve the accuracy of identification of the most viable embryo amongst a less viable sibling cohort, or to



advise patients of chances of pregnancy when only one embryo is available, and no selection is required. Accurate diagnosis of embryo viability can also support treatment strategy, where embryos with higher chance of implantation are transferred singly, thus minimizing the adverse effects of multiple gestation, whereas embryos with low viability can be transferred in multiples, maximizing chance of pregnancy whilst keeping multiple gestation within acceptable levels and maximizing the chance of a healthy live birth per cycle. Currently, embryo viability is diagnosed through morphological assessment of the blastocyst, time-lapse morphokinetic algorithms and PGS. However, morphological assessment of embryos lacks a universal language, with different clinics using different grading schemes to assess their blastocysts. This diversity in blastocyst classification systems has led to confusion for professionals when comparing publications between clinics and for patients when they experience treatment in different clinics. Moreover, morphological assessment of blastocysts has been shown to vary considerably between and within embryologists and clinics. PGS has the drawback of being invasive and only able to achieve an accuracy of about 60%, so that further selection is often required. Time-Lapse has the disadvantage of acquiring a large amount of data, only part of which is utilized for embryo selection. The complexity of time-lapse data means that its full potential as an embryo selection or embryo diagnosis tool, has not yet been reached. The adoption of Artificial Intelligence (AI) to improve healthcare is on the rise. AI applications use a combination of computer programming and mathematics to analyze medical data at a level of complexity that surpasses human cognition. AI provides the potential to become a useful tool to achieve simplified, consistent, accurate and universal embryo selection tool. Since 2010, several AI methods have been used to assess blastocysts. Image segmentation and advanced image analysis techniques using neural networks with textured descriptors, level set, phase congruency, fitting of ellipse methods, have been demonstrated in murine, bovine and human blastocysts. The human publications to date are limited in that they involved low numbers from single centers and no further validation has been published to date. The publications to date relied on images that were captured using inverted microscopes, with only the most recent studies assessing time-lapse imagery. Time-Lapse images have the advantage of being consistent both in terms of image size, lighting, contrast and quality; and in terms of timing of embryo development, particularly important when quantifying blastocyst expansion which is particularly time-dynamic. Deep-Learning of convolutional neural networks has also demonstrated to be a useful tool for embryo selection. The advantage of this technique is that the whole image of the embryo is assessed, not only the pre-determined features segmented, allowing for quantification of all the data available, not just the part we are trained to focus on based on prior knowledge bias. Convolution, therefore, allows the AI to potentially identify patterns in morphological features we did not know to assess. Although AI is not yet in use clinically, the studies to date suggest promising data to support the future use of AI as a routine embryo selection and diagnosis tool, potentially achieving a more simplified, universal and accurate embryo selection tool compared to what is currently available.

THE DEVELOPMENT OF OVARIAN STIMULATION PROTOCOLS FOR IVF

Colin M. Howles

Founder, Aries Consulting Geneva Switzerland and Honorary Fellow, University of Edinburgh, UK

Prior to the start of IVF, pharmaceutical preparations containing biologically active gonadotropins had been in use for about 75 years. Major advances in technology have brought the field of gonadotropin therapy a very long way since the era of animal-, human pituitary (whose use from 1958 for ovulation induction, led

20 years later, to a number of cases of iatrogenic Creutzfeld-Jakob disease (CJD) in material prepared by national agencies from France, Australia and UK)-, and urinary-derived hormones. For almost 30 years, human menopausal gonadotropin (hMG) had been the main gonadotropin available for clinical use. Table 1 lists the characteristics of FSH preparations which have been commercially available. The FSH and LH content of hMG (or menotropin) are equal in terms of biological activity (75IU of FSH and 75IU of LH) as measured by animal derived bioassays. The use of the term IU's and FSH quantities in multiples of 75IU's is still used today even in the era of recombinant gonadotrophins. The early years (1980 to 1995) of ovarian stimulation protocols for Assisted Reproduction were shaped firstly from pioneering work in animal models and then through the use of urinary derived gonadotrophins, in particular menotropin (human menopausal gonadotropin; HMG) and human chorionic gonadotropin (hCG), which were first scientifically described for use together in an IVF ovarian stimulation protocol by Steptoe and Edwards in their landmark 1970 Lancet paper. The use of gonadotrophins for controlled ovarian stimulation will continue to be a cornerstone of a successful ART treatment cycle. The use of segmented ART protocols will gain ground due to the need to reduce the risk of OHSS and also because of concerns about the integrity of the stimulated endometrium to allow implantation. Additionally, vitrification as well as techniques to identify a healthy embryo are facilitating a 'one at a time' embryo replacement policy and a focus on cumulative live birth rates from a single course of ovarian stimulation.

REGULATORY IMPLICATIONS IN THE UK FOR CROSS BORDER MOVEMENT OF FROZEN GAMETES

Nick Jones, UK

Two recently implemented EU Directives (further implementing EU 'mother' Directive 2004/23/EC) concern imports and coding. The import requirement refers to the EU Commission Directive 2015/566 implementing Directive 2004/23/EC regarding the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells. It addresses the importing of tissue and cells into the European Union (EU) from outside the European Economic Area (EEA) and Gibraltar. The coding Directive 2015/565 sets out standards of quality and safety for donation, procurement, testing, processing, preservation and distribution of all human tissue and cells intended for human application. It addresses the procedures to ensure the traceability of tissue and cells following movement within the EU. These requirements have been transposed into the HF&E Act 1990 (as amended) by regulations (the Human Fertilisation and Embryology (Amendment) Regulations 2018) passed by Parliament on 27 February 2018. The regulations come into force in the UK on 1 April 2018. This session updates delegates on the implementation of the Directives – and the challenges in complying with the new requirements faced by UK licensed clinics. The session will also make some observations about the

- import and export of gametes from the EU and third countries, in relation to the United Kingdom
- the availability of gametes from donors within the UK
- The attitudes of patients/recipients to accessing gametes sourced from within, and outside the UK
- The attitude and culture of UK licensed clinics in challenging the status quo.

ACHIEVING DELIVERIES IN PRIMARY OVARIAN INSUFFICIENCY

Kazuhiro Kawamura, *Japan*

In patients with primary ovarian insufficiency (POI), early exhaustion of ovarian follicles was evident due to genetic, immunological, iatrogenic, or other causes. POI affects 1% of women and is characterized by high circulating levels of gonadotropins along with amenorrhea before 40 years of age. They are infertile due to a lack of follicle growth and ovulation; oocyte donation is the only effective treatment option, because residual ovarian follicles in these patients are not responsive to traditional gonadotropin treatments. To induce follicle growth in these remaining dormant follicles, we have developed a method for activation of dormant follicles by using in vitro culture of ovarian fragments treated with PI3K stimulators following disruption of Hippo signaling pathway (IVA, in vitro activation). For IVA approach, ovaries were removed under laparoscopic surgery, and cut into small strips (1 x 1 cm). In each stripe, we submitted 10% volume of ovarian tissue for histological analyses to detect residual follicles. The remaining ovarian strips were fragmented into 1–2 mm cubes before treatment with Akt stimulators (740YP and bpV). If we have some extra ovarian strips, the stripes were vitrified for future treatment. Two days later, the cubes were washed with media without Akt stimulators to avoid introduction of the drugs inside body and then autografted under laparoscopic surgery beneath serosa of Fallopian tubes. Follicle growth was monitored via transvaginal ultrasound and measurement of serum estrogen levels. The patients were treated with FSH until small follicles were developed preovulatory stage followed by hCG to trigger oocyte maturation. Mature oocytes were then retrieved and fertilized with the husband's sperm in vitro before cyropreservation of four-cell stage embryos at day 2. Patients then received hormonal treatments to prepare the endometrium for implantation followed by transferring of thawed embryo(s). When we published second paper in *Human Reproduction* (2015 Mar;30(3):608-15), three pregnancies were achieved based on serum hCG after IVF and embryo transfer. Although one was a miscarriage, two healthy IVA babies have been born with the first one being more than four year of age now. Now, we could have a total of twelve pregnancies. Furthermore, at least eight other pregnancies by three other centers in Spain, China, Poland and Mexico have also been achieved. In this presentation, I will introduce our original IVA procedure and update clinical outcome of IVA so far. Also, I will show some recent projects related to IVA. Especially, I will focus on the new IVA approach, drug-free IVA. The drug-free IVA enables us to increase pregnancy outcome in patients with poor responder/diminished ovarian reserve through the Hippo signal disruption only, leading to stimulation of secondary follicle growth to increase the number of preantral follicles. With appropriate ovarian stimulation, we can expect to increase the number of mature preovulatory follicles in such patients, which contributes to increase number of retrieved oocytes in the IVF protocol.

THE DEVELOPMENT OF IVF IN AUSTRALIA

Gab Kovacs, *Australia*

The development of in vitro fertilisation in Australia for the treatment of infertility began at the Monash University Department of Obstetrics and Gynaecology, at the Queen Victoria Medical Centre in 1971 when Professor Carl Wood recruited Dr. Alex Lopata to establish a human in vitro fertilisation programme to help women with blocked tubes. The only previously reported work on human IVF was from John Rock in the 1940's and Bob Edwards working with Howard Jones in John Hopkins (1966), and also on his return to the UK. The first Australian IVF laboratory was established in Lopata's office at the QVMC where he undertook oocyte cultures, sperm preparations, *in vitro* inseminations, and

the culture of embryos. However, there was a paucity of patients, and Lopata recruited Mr. Ian Johnson at the Royal Womens' Hospital (RWH) to collaborate. At RWH a janitor's storage room near the operating theatres was refurbished as a tiny laboratory. Oocytes were collected by laparoscopy and laparotomy. In 1973 the team achieved its first pregnancy at QVMC. Unfortunately, this pregnancy was "biochemical" and no further pregnancies were achieved from 1973 up to the report of the birth of Louise Brown in July 1978, conceived in a "natural" cycle.

In the meantime, Carl Wood recruited a young animal biologist Alan Trounson, who trained in Jerildere on sheep IVF, followed by time at Cambridge to return to Melbourne funded by a Ford Foundation grant. Whilst Alex worked at both QVMC and RWH, Alan worked only at QVMC. Initially there was little success, but in 1979 two ongoing pregnancies were achieved at RWH. One resulted in the birth of Candice Reed, the world's third confirmed IVF baby, but the other pregnancy was lost after an amniocentesis. Subsequently Alan introduced stimulated cycles using clomiphene citrate at the QVMC and the programme moved its clinical work to St. Andrew's Hospital in East Melbourne. Peter Renou modified the collection needle with a continuous teflon lining. This resulted in a several oocytes being collected for most women, and a better choice of embryos. It was also the practice to replace two or even three embryos. These modifications resulted in the delivery of ten babies (in nine women- including a set of twins) during 1981- the fourth to the 13th confirmed IVF babies in the world- by the Monash team. With the use of stimulated cycles (the Joneses having introduced FSH stimulation to IVF) there was an excess of embryos. To preserve these, Alan Trounson introduced embryo freezing, with the first reported pregnancy in 1983 and birth in 1984. The use of IVF was also extended to male subfertility and unexplained subfertility. As an extension of the treatment of male factor subfertility, microinjection technique was developed by Trounson's team (Lacham 1989) with the technique of Subzonal insemination (SUZI). S C Ng learnt the technique at Monash and returned to Singapore to produce the first birth in the world by this technique. It was subsequently superseded by ICSI. PGD was also developed at Monash but its first successful application was in London with the first birth after embryo sexing. Other advances developed at Monash were invitro maturation and micro-surgical sperm aspiration for obstructive and azoospermia. Rob Jasnsen at Sydney IVF pioneered ultrasound guided trans-cervical GIFT, but this never became popular. Finally commercialisation of IVF was also pioneered in Australia when private equity firm ABN Amro purchased Mon ash IVF in 2007.

INTRACRINOLOGY - THE LACK OF DHEA, THE EXCLUSIVE SOURCE OF SEX STEROIDS AFTER MENOPAUSE BECOMES THE MAIN CAUSE OF MENOPAUSAL SYMPTOMS, INCLUDING VVA

Fernand Labrie

Laval University and EndoCeutics, Quebec, Canada

Problem statement: Demonstration of the clinical importance of intracrinology has started in 1982 with the observation that the prostate synthesizes androgens locally from the circulating inactive steroid precursor dehydroepiandrosterone (DHEA) secreted mainly by the adrenal glands, thus leading to the first treatment to prolong life in prostate cancer and still the best androgen blockade therapy. Three decades of research later, the same intracrinology has been used to identify the main cause of the symptoms and signs of menopause, including vulvovaginal atrophy (VVA), a component of the genitourinary syndrome of menopause (GSM) affecting more than 50% of postmenopausal women. **Methods and Results:** At menopause, the secretion of estrogens stops. Afterwards, DHEA becomes the only source of both estrogens and androgens during all the postmenopausal



years. In order to maintain very low and biologically inactive concentrations of estrogens and androgens in the circulation, DHEA is transformed intracellularly into cell-specific small amounts of estrogens and androgens. Remarkably, over 500 million years of evolution, the peripheral tissues, including the vagina, but not the endometrium, have developed the enzymes able to transform DHEA into small cell-specific amounts of intracellular estrogens and androgens. Most importantly, the estrogens and androgens made inside the cells are also inactivated intracellularly at their site of synthesis, thus practically releasing only inactive metabolites in the circulation, a mechanism which eliminates the risk of an influence in other tissues. The secretion of DHEA, however, has already decreased by an average of 60% at time of menopause and it continues to decrease thereafter with a parallel lowering in available intracellular estrogens and androgens. Consequently, the loss of DHEA becomes practically responsible for the symptoms and signs of menopause. **Conclusion:** Replacing what is missing, namely DHEA, at the right place, at the right time and in the right amount, becomes the logical and physiological approach for the treatment of menopausal symptoms and signs, as recently demonstrated for pain at sexual activity (dyspareunia), the most bothersome symptom of vulvovaginal atrophy due to menopause.

GENE INVOLVEMENT IN MENOPAUSE AND POI

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Menopause is defined as the permanent cessation of ovulation and hence menstruation due to ovarian failure. The median age of menopause is 51 years. However, early menopause might occur at 40 years of age whereas late menopause might happen as late as 62 years of age. Premature menopause is defined as the cessation of ovulation prior to the age of 40 years a condition generally referred to as primary ovarian insufficiency (POI). Menopause is also a highly heritable condition. Genetic variants are known to contribute to about 50% of the variation in age at menopause. Several genetic studies have tried to unravel this genetic background making use of different genetic techniques in population studies as well as in animal models. Genome wide linkage studies have only identified a limited number of genetic variants that seem to be associated with menopause. Population based studies as well as animal research into the genetic background of POI has identified several genetic variants that seem to be associated with primary ovarian insufficiency. However, a lot of these studies suffer from methodological flaws since results are generally not replicated in different independent samples and most of these studies are underpowered. Hence results are conflicting. Recent genome wide association studies (GWAS) have identified numerous genetic variants that are associated with menopause and POI. Genes involved seem to be involved in DNA repair and maintenance as well as in immune function. Biological as well as epidemiological data seem to indicate that reproductive performance, age at menopause and longevity are interlinked through common genetic factors involved in DNA repair and maintenance. In case these systems fail cell death and accelerated ageing occurs. Consequently, ageing of the soma as a result of inefficient DNA repair appears also responsible for failure to reproduce and the subsequent occurrence of menopause. In this way reproductive performance

might be strongly linked to the physical condition of the soma and may be a very good predictor for general health in later life.

NEW INSIGHTS INTO THE PCOS

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Polycystic ovary syndrome (PCOS) is a diagnosis of exclusion, based primarily on the presence of hyperandrogenism, ovulatory dysfunction and PCOM. The syndrome affects 5-20% of women of reproductive age worldwide. Although the condition is characterized by ovulatory dysfunction and polycystic ovarian morphology (PCOM) hyperandrogenism constitutes a key feature of the syndrome. 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. It is unclear whether women with PCOS are also 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. 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. Recently, it became apparent that anti-Müllerian hormone (AMH), which is elevated in women with PCOS, might as well have an effect on the central nervous system in women with PCOS. French researchers were able to show that administering AMH into the midbrain of rats altered the way the GnRH pulse generator was functioning. Doing so increased pulse frequency of GnRH leading to overproduction of LH which in turn increased androgen levels in these rats. Moreover, they also developed polycystic ovarian morphology. Similar data on GnRH neurons and co localizing AMH type II receptors were found in humans. Hence prenatal or postnatal overexposure of offspring to AMH might perturb the GnRH pulse generator inducing PCOS. PCOS seems also to be linked to most of the long-term health issues in that respect that these women have an unfavourable cardiometabolic profile and higher prevalence of CVD risk factors. Moreover, most PCOS patients have a higher chance to develop type II DM and dyslipidaemia. Two recent large cohort studies were not able to establish an increased risk for hard CVD endpoints such stroke, coronary heart disease or myocardial infarction in women with PCOS although all the surrogate markers were without any exception indicating an increased risk for CVD. Moreover, it seems that especially Type II DM and dyslipidaemia are the major drivers for CVD in women with PCOS instead of PCOS itself.



IMMUNOLOGY AND IMPLANTATION

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Background: A unique immune reaction occurs during the implantation window within the endometrium and is essential 1) to promote the embryo adhesion and 2) to regulate the invasion phase. Disequilibrium of such a vital reaction may impede implantation^{1,2}. Documenting the immune environment before conception³ allows to decipher

- The immune mechanism able to generate or at least participate to the observed recurrent embryo implantation failures (RIF) and/ or unexplained recurrent miscarriages (RM)
- And based on the identified mechanism to draw which care personalization may be suitable in function of the immune profile

An equilibrated endometrial environment at the time of uterine receptivity should be theoretically TH-2 dominant with an active mobilization of mature but not cytotoxic uterine NK cells. Women with a history of RIF and/ or RM have specific pre-conceptual endometrial immune deregulations of uterine innate immune cells able to be corrected to enhance their chance of pregnancy at the following embryo transfer. **Participants/materials:** The immune profiling is a diagnostic method detailing from an endometrial biopsy collected in the mid luteal phase the uterine natural killer cells (uNK) mobilization/ activation/ maturation state as well as the local immunoregulated equilibrium between the Th-1 (cytotoxic)/ Th-2 (angiogenic/ immunotrophic) cytokines. The biomarkers IL-15/Fn-14 (maturation and hyper-activation state of uNK) and IL-18/TWEAK (Th-1/ Th-2 equilibrium) mRNA ratios were determined by quantitative RT-PCR and CD56 mobilization per Immunocytochemistry. The objective is to understand if RIF and/or RM are the consequence of an over-immune activation (embryo rejection, apoptosis of the endometrium) or the contrary, of an under-immune activation (no adhesion, low local angiogenesis and immunotrophism) or both (a Th-1 deviation of the endometrial environment with immatures NK cells). In function of the immune profile, care personalization are suggested to counteract the identified mechanisms **Results:** We will present our published^{4,5} and unpublished results in large longitudinal cohort studies and in distinct controlled cohorts studies including RIF patients (after IVF/ICSI or oocyte donation) and unexplained RM. 70 to 80 % of RIF and RM patients show immune deregulations during the implantation window. Our results suggest that personalization in function of the immune profile increases significantly the live birth rate while decreasing the miscarriage rate. We will also show how immunotherapy (corticoids⁶, intralipids) in case of over-immune activation may impact adequately or not the immune profile. **Conclusion:** Uterine immune profiling enables an integrated approach of infertility that includes endometrial immunity as a key factor in planning personalized IVF/ICSI treatments. Understanding the rationale leading to RIF/ RM may use as a guide to personalize of reproductive treatments accordingly. A randomized prospective cohort study is ongoing.

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INCREASED INSULIN RESISTANCE IN MEN WITH UNEXPLAINED INFERTILITY

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This prospective case-control study aimed to test the presence of insulin resistance (IR) in men with unexplained infertility. We included two groups: the study group including 160 infertile men with unexplained oligozoospermia (sperm count <10 × 10⁶/ml) and normal hormonal profile, and the control group of 79 men with proven fertility within the preceding year. A fasting blood test measured IR, FSH, LH, total cholesterol, low-density lipoprotein, high-density lipoprotein and triglycerides. Insulin level was significantly higher in the study group (13.67 ± 10.44) compared with the control group (5.46 ± 3.15), P < 0.0001, and IR was significantly higher in the study group, P < 0.0001. FSH was significantly (P < 0.0001) higher in the study group (4.71 ± 2.57) than the control group (3.15 ± 1.92). LH was significantly higher in the study group (4.98 ± 2.41) compared with the control group (3.15 ± 1.12), P < 0.0001. Total cholesterol was significantly higher in the study group (198.29 ± 37.52) than the control group (182.45 ± 35.92), P < 0.05. In conclusion, IR in men with unexplained

DOES THE TYPE OF HRT MATTER IN POI?

Monica Mittal, UK

Premature ovarian insufficiency (POI) can have both short and long effects on the affected patient population secondary to sex steroid hormone deficiency [1], with a postulated detrimental effect on the overall life expectancy, either secondary to the iatrogenic cause of POI or POI itself, largely due to cardiovascular disease (CVD) [2]. Menopausal women prior to 50 years of age are said to have an increased risk of all-cause mortality (HR 1.12, 95% CI 1.03 – 1.21) and fatal and nonfatal coronary heart disease (HR 1.17, 95% CI 1.02 – 1.35) [3]. These effects may in part be counteracted by oestrogen replacement therapy (ERT), which has been found to lower the risks of CVD and its related morbidity and mortality [4-6]. The cardioprotective role of oestrogens is thought to work through their favourable impact on surrogate markers of CVD such as lipids and lipoprotein profiles [7-8] (reduce low density lipoproteins [LDL] and increase high density lipoproteins [HDL]) [4, 9], endothelial function [10] and their anti-inflammatory and anti-oxidant properties [7, 11-12]. ERT has been shown to improve insulin sensitivity, lower diastolic blood pressure and stimulate the production of vasodilating factors such as nitric oxide [9, 13-14] and prostaglandins by the vessels [9]. The long-term use of oestrogens is thought to lower the risk of mortality by 40% from any cause, but primarily explained by the reduction in the number of deaths seen secondary to CVD [4]. Oestrogen is



commonly available in three different chemical forms: 17 β -estradiol (main ovarian active component); ethinylestradiol (synthetic estrogen); and, conjugated equine estradiol (CEE) (derived from the urine of pregnant mares). Estradiol or CEE are common components of hormone replacement therapy (HRT), whereas the oral contraceptive pill (OCP) contains ethinylestradiol. There is limited evidence comparing these regimens and subsequently there remains considerable variation in practices amongst clinicians. An open-label randomised controlled trial (RCT) assessing the effects of different active ingredients of oestrogen in HRT (Nuvelle [estradiol 2 mg with levonorgestrel 75 mcg; n=12] or COCP [ethinylestradiol 30 mcg with levonorgestrel 150 mcg; n=9]) in women with POI, concluded that HRT was superior to the COCP, but any form of treatment was superior to no treatment at all with regards to bone protection [15]. Furthermore, physiological sex steroid replacement in women with POI results in lower blood pressure, better renal function and less activation of the renin-angiotensin system [16]. The type of progestin used is of paramount importance with the ability of synthetic progestogens to co-interact with a number of different steroid receptors. There are many different classes of progestogens, each with different pharmacological properties dependent upon the parent molecule from which they are derived, testosterone or progesterone, and thus, different side effect profiles [9, 17]. These differences may help to explain why progestogens can partially oppose the beneficial effects of oestrogen [9]. For example, the androgenic properties of some of the progestogens may slightly oppose the HDL-raising effect of oestrogens [9, 13, 18], as well as increase insulin resistance and impair glucose tolerance [4, 14, 19]. Their potency is also determined by the dose, duration and route of administration [13, 20-21]. Micronized progesterone is also referred to as a bioidentical/natural progesterone posing more resemblance to naturally occurring progesterone produced by the corpus luteum than their synthetic counterparts. The bioavailability of micronized progesterone is similar to other naturally occurring steroids [22-23] and is a valid alternative to the older generation of progestogens available on the market [13]. The risk of thromboembolic disease and breast cancer is considered to be lower than with synthetic progestogens [24]. They are also thought to reduce the incidence of new onset diabetes when combined with transdermal oestrogen and have a neutral or beneficial effect on blood pressure in postmenopausal women [25]. Testosterone, in women, naturally occurs in the adrenal glands and ovaries. Testosterone has been implicated in directly improving cardiovascular function (coronary artery dilatation secondary to improvements in endothelial cell function) and indirectly by impacting secondary markers (such as improved exercise tolerance and muscle strength, glucose metabolism and conversion of testosterone to oestrogen) [26]. Many different modalities for HRT administration are available. The mode of administration as well as the progestogens' affinity for the different types of steroid receptors impacts their side effect profile. Godsland et al., (1993) demonstrated that oral combined HRT had a detrimental impact on glucose tolerance, resulting in hyperinsulinaemia when compared with transdermal therapy, despite both regimes containing an androgenic progestogen [9, 27]. The oral route of oestrogen administration also has a greater impact on the lipid profile [28-29] compared to the transdermal route of administration [28].

Randomised controlled trials including the Women's Health Initiative (WHI) study [30], have raised widespread controversy regarding the use of HRT [14]; increasing the risk of coronary heart disease, breast cancer, pulmonary embolism and stroke [31]. However, these trials recruited older post-menopausal women (50 – 79 years of age in the WHI Study) and may have used non-physiological hormonal preparations. It is therefore questionable as to whether this data can be directly extrapolated to counsel younger women who have undergone an early

menopause [12]. Subsequent reports from the same investigators and observational studies have retracted initial claims after re-analysis of the data. Most international guidance documents recommend hormone replacement in women with POI until the average age of the menopause [16, 21, 32-35, 36]. However, there is a lack of data from RCTs regarding the optimal regime for use in this context, and more research is required to further assess this and guide clinical practice [5, 38]. The mainstay of management involves a multidisciplinary approach including counsellors and clinicians [35]. Drug treatments aim to provide physiological levels of the deficient hormones and thus, help minimise the adverse effects of oestrogen deficiency.

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NON ABLATIVE ERBIUM LASER TREATMENT FOR FEMALE STRESS URINARY INCONTINENCE

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Introduction: Stress urinary incontinence (SUI) is a common cause of urinary incontinence and is affecting large number of women influencing significantly their quality of life. There is a large range of therapies for SUI from lifestyle/behavioral modification to surgical interventions, and these therapies differ in terms of both effectiveness and risk. However, current treatment options raised some concerns regarding safety and efficacy and there was a quest for new treatment options. Several years ago vaginal laser therapy was offered as a minimally invasive treatment option for SUI. **Objective:** The purpose of this study was to evaluate long term efficacy and safety of erbium laser treatment for female stress urinary incontinence (SUI). **Methods:** In this single center prospective study in the period from April 2014 to January 2016 we performed ErYAG laser thermo-therapy on a number of female patients having SUI. ICIQ-UI as well as ISI by Klovning were used for assessment of SUI. Patients received two laser sessions with 4-6 weeks interval. Patients' satisfaction was measured with 10 point numerical scale. Follow-ups were performed at 1, 3, 12 and 18 months. Long term follow-ups were performed via telephone interviews during which aside of ICIQ-UI and patients' satisfaction additional questionnaire was used to assess the duration of SUI improvement and patients' readiness to repeat the treatment. Adverse events were registered at every follow-up. **Results:** 132 patients with SUI were included in this study. Average age was 50.3 yrs (range 23-75) and parity 1.9 (range 0-4). Average score on ICIQ-UI before the treatment was 11.8 and at the 3 months FU 3.7, (improvement of 8.1 point). At 3 months FU 39.2% of patients were dry and 96.9% of patients improved their ICIQ score. All reported adverse effects were mild and transient. 75% of patients

have the full effect lasting at least 12 months and 24% at least 18 months. Average duration of full effect was 13.0 months. 85% of patients were not disappointed when the symptoms started to come back. 97% of patients was satisfied with treatment (average score at 18 months was 7.9/10; 68% with grades 8-10 and 41% with 10/10). 98% of patients would repeat the therapy. **Conclusions:** Erbium laser treatment showed efficacy in improvement of female SUI with no major adverse effects noted. Patients' discomfort during the treatment was minimal and satisfaction very high.

GENOME EDITING OF A HUMAN EMBRYO

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Genome editing (CRISPR-Cas or Base Editing) is a revolutionary tool which allows DNA or RNA to be altered at directed loci in the genome with ease and efficiency. The technology, which is derived from and mimics the immune system of bacteria, offers unprecedented ability to alter, correct or insert genes into a genome. The technology has been adopted globally in the research setting and offers limitless potential for personalised medicine; indeed, somatic cell therapies are already benefiting from this technology. The advances in genome editing coupled with assisted reproductive technologies and genomics lend themselves to germline therapy and the correction of genetic disorder in embryos. In order for this to reach the clinic, significant and rigorous testing must be carried out ensure that edits are controllable, reproducible and that mosaicism is avoided. Our research focuses on delivery components of CRISPR, assessing accuracy of edits and measuring mosaicism in edited murine preimplantation embryos.

THE FUTURE OF MINIMALLY INVASIVE SURGERY FOR THE INFERTILITY PATIENT: MAKING MINIMALLY INVASIVE SURGERY EVEN LESS INVASIVE

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The fertility patient is a unique subset of our gynecologic patient population because they tend to be young, active, and healthy. For them it is especially important to resolve their gynecologic conditions in a manner, which will provide them with an effective solution with minimal scars, pain, complications and time off their normal activities. Traditional minimally invasive surgical techniques have begun to address these issues but as technology and surgery evolved, we have to continue trying to make minimally invasive surgery even less invasive. Robotic surgery has changed the field of gynecology because of the advanced instruments that provide not only three-dimensional high definition vision allowing the surgeon to see in even more detail than ever before, with wristed instruments with seven degrees of motion in order to do more complex surgeries with minimally invasive access with increased precision, ease and accuracy. As the familiarity with the robot increases amongst general gynecologists, the rates of utilization have followed a similarly up trending curve. Robotic assisted approaches to myomectomy and endometriosis excision for the fertility patient are increasing in frequency. Another innovation in minimally invasive surgery is the advent of smaller instruments with mini and micro laparoscopic instruments allowing performance of simpler procedures using mini or micro incisions. Mini-laparoscopic instruments include 3 mm trocars, laparoscopes, and mini laparoscopic instruments including scissors, bipolar, graspers, and a suction irrigator. Micro-laparoscopy is performed with trocar-less percutaneous instruments with only a 2 mm skin defect. These instruments allow the performance of cyst and endometriosis excision using



almost scar-less incisions with a much faster recovery and less pain. These instruments also allow hybrid procedures, which include a reduced number of robotic ports with mini or micro instruments replacing the rest. As minimally invasive surgeons we should always be trying to minimize the trauma we cause our patients in order to allow them the fastest recover with the least number and size of scars. Mini-Micro laparoscopy, Hybrid surgical approaches, and robotic surgery all help us to offer less invasive surgical options to most of our patients. This presentation will discuss the future of minimally invasive surgery for the fertility patient and application of various surgical techniques to this patient population.

INTRAVAGINAL PRASTERONE, NOVEL AND NON-ESTROGEN EFFICACIOUS THERAPY FOR VULVOVAGINAL ATROPHY

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Problem statement: Women now spend at least one third of their lifetime after menopause with the high probability of suffering from one or more of the menopausal problems secondary to sex steroid deficiency. With the new understanding of the physiology of sex steroids in women, the logical strategy was to develop a tissue-specific pre-hormone replacement therapy using prasterone.

Methods: The clinical efficacy and metabolism of intravaginal DHEA have been evaluated in six clinical studies, including three 12-week efficacy studies (ERC-210, ERC-231 and ERC-238) using daily intravaginal administration of 0.50% prasterone. In three independent 12-week prospective, randomized, double-blind and placebo-controlled clinical studies, the effect of daily intravaginal 0.50% (6.5 mg) prasterone was examined on four co-primary objectives in women having moderate to severe (MS) pain at sexual activity (dyspareunia) identified as their most bothersome symptom (MBS) of vulvovaginal atrophy (VVA) at baseline. **Results:** In 436 women treated with 0.50% prasterone and 260 women who received placebo, an average 35.1% decrease over placebo in the percentage of parabasal cells ($p < 0.0001$), an average 7.7% increase in the percentage of superficial cells ($p < 0.0001$), and a mean 0.72 pH unit decrease in vaginal pH ($p < 0.0001$) was observed. The severity score of the most bothersome symptom dyspareunia was decreased by 0.46 unit (49%) ($p < 0.0001$ over placebo), whereas the severity score of MS vaginal dryness decreased by 0.31 unit ($p < 0.0001$ over placebo). A very positive evaluation was obtained on the acceptability of the technique of administration of the insert, whereas the male partners reported a very positive evaluation of the changes observed in their sexual partner. **Conclusion:** The data obtained demonstrate the efficacy of intravaginal DHEA on dyspareunia or pain at sexual activity in women suffering from VVA due to menopause. Comparable benefits were observed on vaginal dryness and all the VVA objective signs and subjective symptoms, thus indicating that DHEA corrects the anatomic-morphological VVA changes secondary to the deficiency in sex steroids due to decreasing serum DHEA levels which, in turn, are responsible for the symptoms and signs of VVA. The only observation more frequent in the prasterone groups compared to the placebo groups was vaginal discharge due to increased vaginal secretions in response to treatment with no effect on the endometrium.

SELECTIVE ESTROGEN RECEPTOR MODULATORS (SERMs)

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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. There is an extensive list of compounds that can be considered SERMs for which results are available in either in vitro or in vivo animal cell models and in human experiments. There are more than 60 molecules already described with a SERM-pharmacological profile. Certain phytoestrogens, such as genistein and daidzein, also appear to have a SERM-type pharmacological profile. There are currently three main chemical classes of SERM approved for clinical use: triphenylethylene derivatives, such as tamoxifen and ospemifene, used to treat and prevent breast cancer and vulvovaginal atrophy respectively, and clomiphene to induce ovulation; benzothiophene derivatives, such as raloxifene, used for the treatment and prevention of osteoporosis. And indoles such as bazedoxifene for the treatment of women at risk of osteoporotic fracture. Therefore, the main aim of the pharmacological development of SERMs is to increase the benefit/risk ratio compared to estrogen therapy in the prevention and treatment of several highly prevalent, chronic, postmenopausal diseases that are associated with this state of estrogen deficiency. 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-2 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. Tamoxifen, a drug that was introduced more than 40 years ago for the treatment of hormone-dependent breast cancer, has been considered an anti-estrogen for decades because of its blocking action on the binding of endogenous estrogens to the estrogen receptor (ER) of neoplastic breast cells. However, several studies suggest that tamoxifen may have a protective action on bone tissue (estrogen agonist). Raloxifene is the first SERM approved for preventing and treating osteoporosis. In addition, raloxifene is as effective as tamoxifen in reducing the risk of breast cancer in postmenopausal women and does not significantly affect the risk of cardiovascular disease. Bazedoxifene has been shown to be effective in reducing vertebral and, in a high-risk group, non-vertebral fractures. Finally, the first SERM, ospemifene, has recently been approved in the US and Europe for the treatment of dyspareunia in the US and for patients with vulvovaginal atrophy who are not eligible for estrogen treatment in Europe. This class of drugs has enormous potential in the primary and secondary prevention of various types of estrogen-dependent tumors, postmenopausal osteoporosis and vulvovaginal atrophy.

VAGINAL LASER: ERBIUM OR CO2- WICH HAS SUPERIOR DATA?

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The use of energy-based devices for the treatment of vaginal hyperlaxity, vulvo vaginal atrophy, and stress urinary incontinence, such as minimally ablative fractional laser with CO2 and erbium, is growing and there is more and more experience and data published. Energy-based devices may induce wound healing, stimulating new collagen, and elastin fiber formation. Both



minimally ablative fractional laser CO2 and erbium has been shown to be effective when treating vulvovaginal hiperlaxity and associated secondary conditions, vulvo vaginal atrophy and mild to moderate stress urinary incontinence. These treatments are reported to be safe, effective, and well tolerated with a rapid return to activities of daily living. This review aims to answer clinical question about whether there are differences between the data there is with vaginal laser CO2 versus erbium. A literature review was conducted on technologies in use for feminine vulvo vaginal disorders to explore their safety, efficacy, tolerability, patient satisfaction, and clinical usability. The efficacy and safety of vaginal laser treatment of CO2 versus erbium laser has not been assessed in comparative studies. When you analyze Pubmed (09/01/2018) and put the word laser vaginal, 881 papers appear. If the words you put are (vaginal laser, CO2), 201 papers appear. If you put (vaginal laser, erbium), the number of papers is reduced to 22 and finally if you put (vaginal laser, CO2, erbium), only 2 papers appear. There is no doubt that there are many more studies published with CO2 lasers than with erbium. The use of laser treatment in vulvo vaginal atrophy, vaginal hiperlaxity syndrome and stress urinary incontinence has been described in several studies, all of which used an erbium or a CO2 laser in thermal non-ablative treatment. Improvement rates ranged in vulvo-vaginal atrophy are from 75 to 92% and for stress urinary incontinence from 62% to 78%. No major adverse events were noted. Minor side effects included sensation of warmth; increased vaginal discharge and transient urge urinary incontinence. I will expose my experience with vaginal CO2 laser (SYNERON CO2RE). As this is an evolving medical field, clinical evidence often lacks robustness. Studies and clinical experience suggest that feminine genital disorders using energy-based devices seem an attractive option for patients with mild-to-moderate medical conditions. The treatment can be safely and effectively delivered by trained staff as part of the comprehensive care, that is, currently available to women. But, more rigorous and adequately powered trials are required to assess the relative benefits and adverse event profile of laser treatment of vulvo vaginal atrophy, stress urinary incontinence and vaginal hiperlaxity syndrome as compared with others medical and minimally invasive treatments and procedures.

To date there are no comparative studies between vaginal lasers of CO2 and erbium lasers. If it can be said that both have good results in the mentioned disorders and that the side effects are minimal. Regarding publications, there are practically ten times more publications indexed with CO2 lasers than with erbium lasers.

ICSI: FROM THE BEGINNING TO TODAY, ARE WE OVERUSING IT?

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Ever since its debut in the field of assisted reproductive technology (ART) 25 years ago, intracytoplasmic sperm injection (ICSI) endures the most effective technique to help couples with male factor infertility to conceive. Semen analysis is the first test required for male fertility screening; however, due to its limitations, additional male gamete bioassays such as TUNEL, FISH, PLC \square and pericentriin staining are assessed. The source of spermatozoa used for ICSI can be variable. In the majority of the ICSI procedures conducted at our center, 90% of the cases utilizes ejaculates, including retrograde and electroejaculated specimens, yielding an average of 75.2% fertilization and 41.5% clinical pregnancy rates. The remaining cases, being ICSI not affected by the maturity of male gametes, use microsurgical epididymal sperm aspiration (MESA) and testicular sperm extraction (TESE). As a result, ICSI employing MESA specimens yield 71.2% fertilization and 50.8% clinical pregnancy rates; TESE specimens provide

54.1% fertilization and 40.5% clinical pregnancy rates. Because of the ability to consistently fertilize an egg with an individual sperm cell, cryptozoospermic and poor testicular biopsy specimens may require hours of extensive search to obtain enough spermatozoa to inseminate the oocyte cohort. For these reasons the ICSI procedure is executed by dedicated and well-trained personnel. As per its original intention, ICSI was devised to overcome severe forms of male infertility, and because of its consistent performance, has been extended to non-male factor indications including low oocyte yield, such as in cases of advanced maternal age or poor response to stimulation, PGTA-M, oocyte cryopreservation, and oocyte in vitro maturation. At our center, ICSI is also utilized in a donor egg program and when cryopreserved spermatozoa are used, whether husband or donor. Indeed, since the inception of our ICSI program in 1993, ICSI application has increased from 32.2% to 79.3% in 2016 and continues to gain popularity. This trend has been confirmed by an international survey of the International Committee for Monitoring Assisted Reproductive Technology (ICMART) where in a 3-year period (2008-2010) ICSI cycles have been performed in approximately 67% of 2 million in vitro fertilization cycles, and a similar number of newborns is attributable to this particular insemination method. Like with all other artificial reproductive techniques, there is a concern that ICSI may propagate genetic defects already present in a family, or even more pressing is the concern related to eventual epigenetic modifications appearing in the progeny, there is a need for more follow-up studies to continue monitoring offspring health and development. As we continue to strive to identify embryo developmental competent gametes, we endeavor to gain more insights into their genomic and epigenomic composition.

CHOICE OF PROTOCOLS FOR PREGNANCY SUPPORT

Roberto Palermo, Italy

In spontaneous conception, successful embryo implantation and endometrial decidualization are necessary for providing the necessary required necessary for providing maternal support of developing embryo(s). Human reproduction is highly inefficient process compared to other primates. In women, the average chance of pregnancy is only 15% per cycle during their lifespan. In the contest of Assisted Reproductive Technologies (ART), approximately 25% of transferred embryos will implant. Usually ART implicates a series of hormonal manipulation of natural ovarian and endometrial cycle, determine various degree of hormonal inadequacies, during the postovulatory (or post-oocytes retrieval), thus producing the need of pharmacological strategies for pregnancy support. Different scenarios may be described in which different possible protocols for pregnancy support have been proposed, evaluated and compared:

- Various strategies of induction of multiple follicle development (essentially GnRH-analogue-gonadotropins coadministration→hCG induction of final oocytes maturation→oocyte retrieval→ IVF/ICSI→and fresh embryo transfer;
- Induction of multiple follicle development with Gonadotropins/GnRH-antagonist→GnRH-agonist trigger for the final oocyte maturation→oocyte retrieval→fresh embryo transfer or freeze all strategy of oocytes and/or embryo(s) for postponed embryo transfer;
- Pregnancy support after postponed embryo transfer with thawed oocyte(s) and/or embryo(s). this latter scenario requires endometrial preparation either in spontaneous ovulatory cycle pharmacological preparation of endometrium.

The luteal phase is known to be abnormal in all the ART cycles involving ovarian stimulation. It is assumed that this luteal-phase inadequacy is associated with the supra-physiological



concentrations of oestradiol and progesterone due to multifollicular development. The high steroid concentrations have a negative feedback on the hypothalamic–pituitary axis, resulting in suppression of LH secretion. LH activity plays a crucial role in the luteal phase, since it stimulates implantation and is entirely responsible for the steroid activity of the corpus luteum. Progesterone is the central component of all protocols for pregnancy support associates with ART. Either directly administered in various pharmacological preparation (progesterone in oil or hydro soluble preparations; micronized, including also dydrogesterone) or via stimulation of endogenous secretion with hCG or GnRH-agonist. Different route of administration of different agents (intramuscular, oral, vaginal, rectal, subcutaneously) have been proposed and compared. Considering that oestrogens are a component of the hormonal secretion from the corpus luteum, oestrogens have also been used for pregnancy support (oral, transdermal or vaginal administration). In a recent Cochrane review a higher rate of ongoing pregnancy/delivery was reported when progesterone was used. According the Authors' conclusion of this metanalysis, "*hCG or progesterone given during the luteal phase may be associated with higher rates of livebirth or ongoing pregnancy than placebo or no treatment, but the evidence is not conclusive. The addition of GnRH α to progesterone appears to improve outcomes. hCG may increase the risk of OHSS compared to placebo. Moreover hCG, with or without progesterone, is associated with higher rates of OHSS than progesterone alone. Neither the addition of oestrogen nor the route of progesterone administration appears to be associated with an improvement in outcomes*". Nevertheless, the level of evidence was stated as "*very low quality*".

The use of Clomiphene Citrate (CC)

The majority of the studies performed in cycles stimulated with clomiphene/human menopausal gonadotrophin observed abnormal endometrial development endometrial advancement on the day of oocyte retrieval has been reported to decrease the chance of pregnancy. The use of CC is apparently associated with a luteal defect; despite the treatment with CC is performed in the follicular phase. This is demonstrated by the lack of sufficient LH concentrations in the luteal phase, the similar progesterone concentrations and the asynchronous endometrium in the majority of the patients. Therefore, additional treatment with CC does not seem to be a valid alternative for standard treatment, and adequate pregnancy support.

Timing of pregnancy support (initiation of P4)

The results of one recently published systematic review, suggest that the timing of luteal progesterone support initiation can affect the chances of reproductive success. Studies performed on luteal support initiation before oocyte retrieval compared with the day of oocyte retrieval, suggest a potential decreased likelihood of pregnancy if progesterone was initiated before oocyte retrieval. When progesterone was initiated on the evening of oocyte retrieval compared with days 1–3 after oocyte retrieval, studies found no difference in clinical pregnancy rate. One study investigated progesterone initiation on day 3 or 6 after oocyte retrieval and reported a decreased likelihood of pregnancy on day 6 initiation. These results suggest a window between the evening of oocyte retrieval and day 3 after retrieval as the ideal time for initiation of progesterone. Multiple factors affecting P timing and serum levels during the luteal phase in ART cycles have been proposed. These include endometrial advancement from "premature" progesterone activity, disruption of granulosa cells (GCs) during oocyte retrieval, pituitary down-regulation or blockade of GnRH receptors, hypothalamic suppression of GnRH, method of oocyte maturation induction, and differing routes of progesterone administration.

Timing of pregnancy support (when to stop)

Regarding discontinuation of hormonal pregnancy support, some investigators limited supplementation to the day of a positive β -hCG while others continued treatment up to 12 weeks of

pregnancy. It has recently been reported, in a prospective study, that prolongation of progesterone supplementation for 3 more weeks beyond the day of a positive pregnancy test had no influence on miscarriage rates and concluded that progesterone supplementation can safely be withdrawn at the time of a positive hCG test. Despite the lack of evidence to support continuation of pregnancy hormonal support beyond the day a clinical pregnancy is established, many believe that progesterone supplementation should be continued up to the 10th week of gestation. Although comparative studies have generated relevant data, evidence and knowledge about the reproductive functional dynamics in ART, emerging data demonstrate that there is a wide individual variation in luteal-endometrial function especially in relation to the hormonal manipulation associated with ART. Therefore, the need of tailored strategies for pregnancy support require the search markers for a better patient's selection and treatment.

PREMATURE OVARIAN INSUFFICIENCY GLOBAL REGISTRY TO OPTIMISE MANAGEMENT

Nick Panay, UK

Context: Premature ovarian insufficiency (POI) remains poorly understood and under-researched. Recent published guidelines from ESHRE, IMS, EMAS and NICE UK have been developed using data largely from observational and short term randomised studies. The POI registry <https://poiregistry.net> has been developed at Imperial College London, UK using a British Research Council grant to collect national and international data in an effort to avoid fragmented research and improve our understanding of this relatively uncommon but important disease.

Objective: Retrospective and prospective registry analysis of women with POI. **Methods:** Data collected on women diagnosed with POI younger than 40 years have been entered onto an online registry utilising the semantic web. The data were subsequently extracted and analysed at Imperial College London by patient ages, aetiology, ethnicity, time to diagnosis, symptom profile and bone mineral density (BMD). **Results:** 45 centres have registered to enter data globally thus far. Many of the centres are in the UK but also include investigators in Australia, Canada, Chile, China, Italy, Spain and South Africa. Retrospective (legacy) data have been entered for 484 women and prospective data for 343 women with POI thus far. Data entry include demographics, diagnosis, presentation, management and outcomes such as bone mineral density. Collaborative work is being conducted to facilitate biobanking for genetic and biomarker analyses. A key finding from early data analyses is that delay to diagnosis results in lower bone mineral density. These and other data on diagnosis, presentation and management of POI will be presented at the 26th World Congress on Controversies in Obstetrics and Gynaecology and Infertility (COGI) in London, Nov 23rd-25th, 2018. **Conclusions:** The POI registry has already proved successful in data collection as shown by the number of centres registered and the number of patients entered thus far. By encouraging more healthcare professionals to engage with data collection, we aim to optimize the quality and quantity of data. It is particularly hoped that a long and successful global partnerships will be achieved to improve the diagnosis and treatment of premature ovarian insufficiency.

HORMONE THERAPY REGIMENS – ARE THEY ALL THE SAME?

Nick Panay, UK

The adverse outcomes seen in The Women's Health Initiative (WHI) combined hormone therapy trial were mainly to an over-dosage of menopause hormone therapy (MHT) in a relatively elderly population. However, fundamental differences exist between conjugated equine estrogens and 17 beta estradiol and



between medroxyprogesterone acetate and other progestogens. It is likely that these differences also contributed to the adverse outcomes in WHI, which were contrary to the cardiovascular benefits seen in previous observational trials. In addition to binding to the progesterone receptor, many progestogenic compounds also bind to the glucocorticoid, mineralocorticoid and androgen receptors. This can lead to unwanted effects such as unfavourable glucose metabolism, fluid retention, acne, weight gain. Recent studies of cardiovascular risk markers in younger women have therefore been designed using predominantly 17 beta estradiol and progesterone or dydrogesterone as primary interventions. Menopause societies are now advising that natural progesterone and dydrogesterone may have more favourable metabolic and breast effects compared to synthetic progestogens. Natural progesterone and dydrogesterone do not attenuate the beneficial effects of estradiol in reducing insulin resistance and arterial compliance. There also appear to be differential effects of progesterone and progestogens on breast tissue. Progesterone has a neutral and dydrogesterone a pro apoptotic effect on breast epithelial cells, whereas androgenic progestogens such as medroxyprogesterone acetate appear to have a proliferative effect, possibly through non specific effects on the glucocorticoid receptors and gene expression. This might explain the small increase risk in breast cancer promotion in some studies when synthetic progestogens are combined with estrogen. Observational data such as the French E3N cohort and the Finnish registry cohort suggest that women using natural progesterone and dydrogesterone are not at increased risk of breast cancer within the first 5 years of use; ideally these data will be confirmed in the future by definitive long term, randomised prospective studies. Thus, replication of the physiological hormonal environment with estradiol and favourable types of progestogens and progesterone can maximise benefits and minimise side effects and risks of MHT. It is time we moved away from the notion, often propagated by epidemiologists and the media, that all hormone therapy products have a single class effect.

HRT: CLINICAL DATA AND INTERNATIONAL GUIDELINES

IMS Recommendations on women's midlife health, "POI" and menopause hormone therapy

Nick Panay

on behalf of

R. J. Baber, N. Panay, A. Fenton and the IMS Writing Group, UK

The International Menopause Society (IMS) has produced the 2016 recommendations on women's midlife health, "POI" (premature ovarian insufficiency) and menopause hormone therapy (MHT) to help guide health-care professionals in optimizing their management of women in the menopause transition and beyond. The term MHT was used to cover therapies including estrogens, progestogens and combined regimens. For the first time, the IMS recommendations include grades of recommendations, levels of evidence and 'good practice points', in addition to section-specific references.

Where possible, the recommendations are based on and linked to the evidence that supports them, unless good-quality evidence is absent. Particular attention has been paid to published evidence from 2013 onwards, the last time the IMS recommendations were updated. Databases have been extensively searched for relevant publications using key terms specific to each specialist area within menopause physiology and medicine. Information has also been drawn from international consensus statements published by bodies such as the IMS, the European Menopause and Andropause Society and the North American Menopause Society. The recommendations have been produced by experts derived mainly from the IMS, with the assistance of key collaborators where deemed advantageous. In preparing these international recommendations, experts have taken into account geographical

variations in medical care, prevalence of diseases, and country specific attitudes of the public, medical community and health authorities towards menopause management. The variation in availability and licensing of MHT and other products has also been considered.

GENERATING AN HPV DIAGNOSIS IN A SCREENING EVENT

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Primary screening for high-risk HPV genotypes (hrHPV) generally detects more CIN2, CIN3 or cervical cancer compared to cytology at cut-off ASC-US or LSIL, but is less specific. According to the last European guidelines for quality assurance in cervical cancer screening, primary HPV testing can be used only in a population-based program for cervical cancer screening; HPV testing outside such programs is not recommended. When designing an HPV test to be used for primary cervical screening, the ultimate sensitivity for the detection of precancerous lesions by inclusion of HPV types that are rarely associated with cervical cancer, must be carefully weighed against the potentially dramatic loss of clinical specificity when a particular HPV type (e.g., HPV53 and HPV66) is frequent in low-grade disease or in women without disease. In addition, it should always be taken into consideration that absolute reassurance following a negative cervical cancer screening test result is not achievable at any analytic sensitivity, because of a myriad of factors that are independent of the actual screening test performance, including operator error and poor cervical sampling. Thus, a cervical cancer screening program should adopt an HPV test for use as screening tool, only if it has been validated by demonstrating reproducible, consistently high sensitivity for CIN2+ and CIN3+ lesions, and only minimal detection of clinically irrelevant, transient HPV infections. There is a consensus in the HPV community that HPV tests (neither commercial nor in-house tests) that have not been clinically validated should not be used in clinical practice. HPV testing should be performed only on samples processed and analyzed in qualified laboratories, accredited by authorized accreditation bodies and in compliance with international standards. Laboratories involved in HPV-based screening should perform a minimum of 10,000 HPV tests per year. Several comprehensive inventories of commercially available HPV tests were published in the last decade. As of September 2018, at least 250 distinct commercial tests for detection of alpha HPVs and at least 230 variants of the original tests are available at the global market. Unfortunately, only a subset of commercial HPV tests has documented clinical performance for agreed indications for HPV testing in current clinical practice. For more than half of HPV tests in the global market, no single publication in peer-reviewed literature can be identified. In contrast to commercial kits for "classical" molecular microbiology targets, the great majority of HPV commercial tests currently on the market do not contain a sample extraction step and a number of them do not even mention recommended nucleic acid extraction methodology in their manufacturer's instructions. Only a minority of HPV tests on the market have internal controls. As a multitude of hrHPV tests are available, regularly updated evaluation of their suitability for primary cervical cancer screening is essential. A recent systematic review, listed the hrHPV DNA tests that were either validated through randomized trials showing a very low incidence of cervical cancer after a negative hrHPV DNA test or fulfilling consensus based international equivalence criteria based on cross-sectional data. The international equivalence criteria are based on the non-inferior cross-sectional accuracy of a new HPV test versus one of the two benchmark comparator tests (GP5+/6+ PCR-EIA and/or Qiagen Hybrid Capture 2 HPV DNA Test) that have been validated in clinical trials and detect the same molecular targets, i.e., DNA of hrHPV types. To fulfil the necessary criteria, the candidate test should



demonstrate a relative sensitivity and specificity to detect CIN2+ compared to the standard comparator tests of more than 0.90 and 0.98 respectively, and show high inter- and intralaboratory reproducibility. Other potential cervical cancer screening tests based on other target molecules such as HPV mRNA, proteins or methylation markers cannot directly be considered equivalent and require additional evidence regarding their longitudinal effects, i.e., long-term safety. The proper validation of HPV DNA tests, according to the international equivalence criteria can be problematic due to difficulties with obtaining an appropriate set of clinical specimens. The recently launched international framework "Validation of HPV Genotyping Tests (VALGENT)" facilitates the comparison and validation of HPV DNA tests by providing a set of samples obtained from women attending routine screening (1,000-1,300 samples) enriched with cytologically abnormal samples (300 samples). In order to allow comparison with other HPV tests, each VALGENT panel includes a comparator assay that is previously clinically validated for cervical cancer screening purposes. As of September 2018, only 14 commercial HPV assays (out of +480 HPV assays at the global market) can be considered as completely or partially validated for primary HPV-based cervical cancer screening. Since the performance of an HPV test may vary depending on the sample collection procedures and medium, regulatory approval in some settings requires validation of performance based on the choice of sample collection medium. Importantly, the validation of a pre-approved assay for use with a specific medium is a simpler process than de novo clinical validation of an HPV assay. It can be expected that several previously approved tests will eventually be validated for use with the most commonly used collection media. It is worth to mention, that although we have an increasing understanding of which HPV tests are valid for HPV-based primary cervical cancer screening, given an internationally accepted and applied validation framework and published professional guidance, we do not have widely accepted equivalent metrics to judge the validity of HPV tests in other clinical settings, including post-treatment surveillance and the triage of low-grade abnormalities. International efforts to create such validation guidelines will be of great benefit, since existing data show significant variation between commercially available.

THE ALTERNATIVE MANAGEMENT OF UTERINE FIBROIDS IN INFERTILE PATIENTS

Nicole Sanger, *Germany*

Fibroids are the most common benign gynaecological tumours in women and they affect mainly women of reproductive age. Beside the classical symptoms such as bleeding disorders or pressure/pain in the lower abdomen, fibroids can also lead to infertility. If other subfertility factors are excluded, the question has to be posed if the fibroids warrant treatment and if so, how and at what time the treatment should be performed. These decisions are usually dependent on their number, size, and location and if there is an impairment of the uterine cavity. Another important aspect that should be taken into account when considering the requirements for a pregnancy is the age of the patient. Ovarian reserve, age/quality of the oocytes and the required time after therapy until a pregnancy may occur, must be included in the decision-making process. All potential methods need to be assessed, as the commonly performed myomectomy is not the appropriate therapy for all patients. These alternative methods should include other interventional options such as Uterine Artery Embolization (UAE) or Sonographic/Magnetic Resonance Guided High Intensity Focused Ultrasound (HiFUS) and more importantly medical therapy with GnRH, ulipristal acetate (UPA), oral contraceptives, or Levenorgestrel-containing IUD. While there are data showing a clear benefit regarding the onset of pregnancy or IVF outcomes after myomectomy, the alternative methods

mentioned have to also be considered in order to assess the potential risks against their benefits – not only for the probability on pregnancy but also for possible pre-, peri- or postpartum complications. An embolization of the uterine artery (UAE) is mainly an option to be considered for women who have no desire to get pregnant as it may increase the risk of premature menopause. and AMH and ovarian reserve have been reported to be significantly lower after embolization. Furthermore, pregnancies after embolization are more often complicated with increased miscarriage, premature labor, placental problems and anomalies, which explains why the indication for infertile patients must be critically evaluated before use. Adding to the controversy around the use of UAE, normal pregnancies have been reported in literature resulting in a confusing picture of the benefit of this technique in this population. High Intensity Focused Ultrasound (HiFUS), guided by MRI or ultrasound, uses ultrasound waves focused in one area resulting in a temperature increase to 57 - 80 °C, which in turn causes coagulation with necrosis in the fibroid. The results of this technique are not consistent and additional surgical interventions are often required. This technique is not suitable for stemmed and intramural fibroids, has a limited working area and is not applicable in obese patients. Pregnancies have been reported, most often in case series or in retrospective observational trials, without negative impact on miscarriages or obstetrical outcome. However, as data from prospective trials are lacking, the impact of HiFUS on fertility cannot be estimated. Regarding non-invasive medical therapies, contraceptive methods only have an effect on fibroid-related symptoms, whereas therapies such as GnRH and UPA both additionally can lead to shrinkage of fibroids. Due to the known side effects of GnRH caused by the reduction in the estrogen levels (such as vasomotor symptoms and low bone density), treatment with UPA is becoming increasingly important in women who wish to become pregnant, and is offered to patients in both the preoperative setting as well or as long-term intermittent therapy. The use of UPA has a proven benefit regarding reduction in size and volume of fibroids over a 3 months treatment period. It induces apoptosis by a direct action on the progesterone receptor in the fibroids, often leading to a permanent decrease of the volume. The repeated administration of UPA also has a cumulative effect on the decline in size of the fibroids, making surgery unnecessary in many cases. Pregnancies after administration of UPA have been reported, but prospective studies including a larger series are pending. While the histological safety of UPA on the endometrium is well documented, the potential influence of UPA on the endometrial receptivity as well as on the implantation of an embryo is still to be fully assessed. Individualized treatment in the case of uterine fibroids is a key to a successful pregnancy. Making an informed decision on the best option is the responsibility of an interdisciplinary team as surgical outcome depends on the surgeon's skills, HiFUS and UAE require the presence of an experienced radiologist, and preserving ovarian function with the use of medical therapy such as UPA/GnRH lies within the expertise of reproductive gynecologists. The balancing of all these options, and the assessment of the benefit versus the risk should be considered to result in the best outcome for the patient and the highest chance of a resulting successful pregnancy.

WHO CLAIMS, "ESTROGENS ARE CARCINOGENIC – A DIFFERENTIAL APPRAISAL"

Christian Singer, *Austria*

Compelling evidence suggests that estrogen exposure is an important determinant of breast cancer risk. The mechanisms by which estrogens initiate and promote carcinogenesis in the breast are include the generation of genotoxic and mutagenic metabolites, tissue irritation, and the stimulation of tissue growth. Furthermore, an association between the breast cancer risk and



elevated blood levels of estrogen has consistently been found in many observational epidemiological studies. These studies also suggest that hormone replacement therapy is associated with a small but significant (albeit reversible) increase in the risk of breast cancer, and that estrogen replacement may have a similar effect. However, because of the study-inherent heterogeneity of subjects and treatment strategies used, the clinical relevance of these findings is unclear, as well as the role of potential carcinogenic co-factors such as progestins. This question was addressed in the Women's Health Initiative study, a prospective trial in which post-menopausal women were randomly assigned to receive placebo or hormone-replacement therapy (HRT) or either placebo or estrogen-replacement therapy in case they had undergone hysterectomy. The study was closed prematurely because of an increase of breast cancer and cardiovascular endpoints. However, while more recent follow up data confirm the unfavourable side effect profile of progestins-combinations, estrogen alone had no effect on breast cancer risk or breast cancer-related mortality. While in women with an intact uterus, estrogen-progestin combinations pose a statistically significant increase in breast cancer risk, the risk is comparable to postmenopausal obesity, nulliparity, or increased breast density. Considering the clear evidence that menopausal hormone therapy provides a superior relief of menopausal symptoms, national and international guidelines (such as the NICE guideline on menopause) therefore recommend the consideration of HRT in symptomatic patients as a therapeutic option.

SURGICAL MANAGEMENT OF MULTI-ORGAN ENDOMETRIOSIS AND PREGNANCY OUTCOMES Theirs Raymundo Soares, USA

Endometriosis is a disease characterized by the presence of glands and stroma in topography other than the uterine. Dysmenorrhea, dyspareunia and infertility are among the main complaints reported by these patients. Transvaginal ultrasonography and magnetic resonance imaging of the pelvis, both with bowel preparation, are the main imaging methods used in the preoperative evaluation of these patients. In infertile patients, drug therapy has no beneficial effect for reproductive purposes. Surgery and assisted reproductive therapy are the treatments used in an attempt to improve the outcome of pregnancy and the live births. Age, ovarian reserve, degree of pain and functional impairment of the pelvic organs are some of the characteristics evaluated to decide between the surgical procedure or the treatment with the infertility specialist. Both play a key role in improving reproductive rates. During this presentation, we will discuss the main surgical techniques used for the treatment of patients with deep endometriosis and the main studies on their impact on the fertility of these women.

DOES RIF EXIST? Edgardo Somigliana, Italy

The definition of Repeated Implantation Failure (RIF) remains controversial. Several different proposals have been suggested but a consensus has not yet been reached. The two main factors commonly included in the proposed definitions are the number of failed cycles and the quality of the transferred embryos. The most common proposed definitions are based on a number of failed cycles of two or three and refer to women at good prognosis (young age and good quality of the transferred embryos). In fact, the main and unsolved diagnostic challenge is discerning between women who are just unlucky and those who harbour some obscure and yet not identified medical conditions that are detrimental to embryo implantation. In this scenario, it is of utmost importance taking into consideration the basic rules of probability

distributions. In a recent model, it has been shown that in population of women at good prognosis (30% chances of pregnancy with IVF), the chances to misclassify women as affected by RIF (while they are just unlucky) is 81%, 75% and 51% after two, three and six failed cycles respectively. In other words, after 6 failed cycles only one of two women is actually affected by a condition interfering with embryo implantation. In a population at maximal prognosis (pregnancy rate of 50%, such as those undergoing oocytes donation), the inaccuracy remains high after two or three attempts (69% and 53% chances of false positive diagnoses, respectively). Only after six cycles, the chances of misdiagnoses dropped to 12%. On these bases, one can reasonably conclude that the vast majority of women currently labelled with a diagnosis of RIF is actually perfectly healthy and does not deserve any particular investigations or treatments. They just need to perform new cycles. Unfortunately, this high rate of misdiagnoses is not without consequences. Couples are frequently disparate after two-three failed attempts and strongly request for new investigations and treatments. This can cause wastage of financial resources and may expose couples to unjustified additional risks. From a clinical perspective, there is the need for a patient-friendly approach aimed at ensuring adherence to repeated cycles and reducing drop-outs. From a research perspective, there is the need to investigate the causes and possible treatments of RIF in highly selected women (6 failed cycles in good prognosis women?) in order to obtain robust and meaningful evidence.

OVARIAN ENDOMETRIOMA BEFORE INFERTILITY: PREFER IVF FIRST? Edgardo Somigliana, Italy

Surgery and IVF are two radically different approaches. In the first scenario, the woman should undergo surgery and then seeking for natural conception for up to one year, while, in the second one, she should undergo 3-6 cycles of IVF. For both approaches, women and their partners have to play an essential and active role. Adherence is actually essential for both. For this reason, decision between surgery and IVF should emerge from a shared decision-making process with the couple. An appropriate counselling is thus fundamental. But what are the main information that should be offered to the couple? Based on the available literature, the counselling should include the following main information: 1) Surgery improve natural fecundity but the magnitude is presumably modest (25% of couples conceive in one year), 2) The chances of pregnancy with IVF is about 25% per cycle, 3) Surgery may damage the ovarian reserve (10-15% of ovaries are compromised after surgery) and this can impair IVF success, at least in women with bilateral endometriomas; 4) Both surgery and IVF expose women to risks (even if the type of risks differ), 5) Surgery improve pain symptoms (if present) but does not protect from recurrences; 6) Second surgery is poorly effective (if not ineffective) in terms of enhanced fertility, 7) Even if one may intuitively think that ovarian reserve can be progressively damaged over time by the presence of ovarian endometriomas, evidence is scanty and controversial, 8) Large endometriomas (> 4 cm) can impair ovarian responsiveness but small ones are unremarkable, 9) Endometriomas can cause peculiar complications of IVF (infection and development of ovarian abscesses in particular) but this is very rare. In clinical practice, couples who receive this information tend to opt for IVF. The lower chances of pregnancy with surgery (and the shorter time to pregnancy) and the atavistic fear of surgical interventions may be the essential reasons. In other words, women know what is best for them. The debate between surgery and IVF is a mere never-ending intellectual debate among physicians.

HRT FOR PRIMARY PREVENTION?

John Stevenson, UK

Oestrogen deficiency is a major risk factor for coronary heart disease (CHD), and hence hormone replacement therapy (HRT) in postmenopausal women was expected to prevent CHD. Studies of different HRT regimens have been undertaken to demonstrate their effects on surrogate markers of CHD risk. Beneficial effects of HRT on lipids and lipoproteins and on glucose and insulin metabolism have been demonstrated, although these will vary according to the type of progestogens used. Progestogens with androgenic properties, such as norgestrel and medroxyprogesterone acetate (MPA), may oppose the metabolic benefits of oestrogens whereas this is not seen with non-androgenic progestogens such as micronized oral progesterone and dydrogesterone. The route of administration of HRT may also be important in terms of prothrombotic effects, although this may also be dose dependent. Direct arterial effects of oestrogen are clearly important and are largely beneficial, whilst influences on vascular remodelling are dose dependent. Thus, inappropriately high doses of oestrogens have the potential to be adverse for the cardiovascular system, and the dose at initiation of therapy must be carefully chosen according to the age of the patient. Many observational studies have shown an association between postmenopausal HRT use and a reduction in CHD. However, some randomised clinical trials of HRT have shown only neutral effects, particularly in the secondary prevention of CHD in women with established disease. The largest primary prevention trial was the Women's Health Initiative (WHI) which included over 27,000 postmenopausal women. WHI initially purported to show that HRT significantly increased coronary events in postmenopausal women compared with placebo. With subsequent publications of the complete data from WHI this finding turned out to be incorrect. Overall there was a small non-significant increase in CHD events with HRT comprising conjugated equine estrogens (CEE) plus MPA and a small non-significant decrease in CHD events with HRT comprising CEE alone. Previous animal studies had shown that CEE started at the time of menopause significantly reduced atheroma development compared with placebo, but if the initiation of CEE was delayed by the equivalent of 5 human years this protective effect was not seen. When the WHI data were appropriately analysed according to age at initiation of therapy, as per protocol, there was a significant decrease in CHD events in the cumulative follow-up seen with CEE alone use compared with placebo in women initiating therapy below age 60 years. This was not seen in the women randomised to CEE plus MPA, thereby showing a detrimental effect of this particular progestogen. Benefit for CHD was also seen in the Danish Osteoporosis Prevention Study (DOPS). This was a clinical trial of 1000 women soon after the onset of menopause who were randomised to oral oestradiol 17- β , plus norethisterone acetate if non-hysterectomised, or to no treatment. The trial ran for 10 years with a 6-year subsequent observational follow-up and showed a significant reduction with the HRT in a composite endpoint of myocardial infarction, death or heart failure. Meta-analyses of randomised clinical trials of HRT and CHD provide much greater patient numbers, between 30,000 and 40,000 women, and such studies have shown significant reductions in CHD events if the HRT was initiated below age 60 years. Initiation above age 60 years resulted in neither benefit nor harm. These findings are supported by studies of over 90,000 women from the Finnish National Register which have shown significant decreases in CHD mortality with HRT use initiated below age 60 years, and non-significant decreases seen in those initiating HRT above age 60 years. In keeping with this, they have also shown that stopping HRT results in a transient increase in CHD mortality. The totality of current evidence strongly suggests that HRT is effective for the primary prevention of CHD in postmenopausal women. Critical to this is the timing of the intervention, the dose at initiation, and the types of hormones used

in the HRT regimen. Primary prevention should now become a recognised indication for HRT use.

RISK OF CANCER IN WOMEN AND CHILDREN AFTER ART

Alastair Sutcliffe, UK

Resilience factors are those which determine overall life expectancy and were well recognised by the work of the late David Barker and others. In an ESHRE working group in Winchester he was presenting and showed a slide of woman celebrating her 99th birthday using a cigarette to light her candles. He said she would have been a large health birthweight with a health Mother. So resistant to the effects of smoking (50% of those who smoke die from a smoking related illness, but the other 50% don't) Resistance to cancer is a form of biological fitness or resilience. So, what about children conceived after ART and women who have been treated (exposed to) ART. Does this increase their risks of cancer? Thus, so giving a bellwether as to their future longevity. The author will present two worlds' largest studies. One investigates the risk of children getting cancer before the age of 15 in Great Britain and involved a study of 106,000 children. A further study asking that question of 22,000 children born after donor gametes will also be presented. Next will be a study of the women in the UK treated between 2010 and 1991 with ART cycles and will report rates of ovarian, breast and corpus uteri cancers in this group. In the childhood cancer study there is good news, no more cancer than the population as a whole, in the women's cancer study most evidence suggests the same although there are small increased risks of ovarian cancer described. And that involved 2.2 million women years of exposure and 302,000 women.

DOES COCHRANE REVIEWS SHOW ANY ROLE FOR METFORMIN IN THE MANAGEMENT OF PCOS?

Thomas Tang, UK

Background: Polycystic ovary syndrome (PCOS) is characterised by menstrual disturbance, hyperandrogenism and hyperinsulinaemia. Hyperinsulinaemia occurs secondary to insulin resistance and is associated with increased risk of cardiovascular disease and diabetes mellitus. Insulin-sensitising agents such as metformin may be effective in treating PCOS-related anovulation. **Objectives:** To evaluate the effectiveness and safety of metformin improving reproductive and metabolic outcomes for women with PCOS undergoing ovulation induction. **Search methods:** We searched the following databases from inception to January 2017: Cochrane Gynaecology and Fertility Group Specialised Register, CENTRAL, MEDLINE, Embase, PsycINFO and CINAHL. We searched registers of ongoing trials and reference lists from relevant studies. **Selection criteria:** We included randomised controlled trials of insulin/metformin compared with placebo, no treatment, or an ovulation-induction agent for women with oligo and anovulatory PCOS. **Data collection and analysis:** Two review authors independently assessed studies for eligibility and bias. Primary outcomes were live birth rate and gastrointestinal adverse effects. Secondary outcomes included other pregnancy outcomes, menstrual frequency and metabolic effects. We combined data to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs). We assessed statistical heterogeneity using the I^2 statistic and reported quality of the evidence for primary outcomes using GRADE methodology. **Main results:** We assessed the interventions metformin, clomiphene citrate, metformin plus clomiphene citrate. We compared these with each other, placebo or no treatment. In total, 42 studies (4024 women) were included in the analysis. **Metformin versus placebo or no treatment:**

The evidence suggests that metformin may improve live birth rates compared with placebo (OR 1.59, 95% CI 1.00 to 2.51, 4 studies, 435 women, $I^2 = 0\%$, low-quality evidence). The metformin group experienced more gastrointestinal side effects (OR 4.76, 95% CI 3.06 to 7.41, 7 studies, 670 women, $I^2 = 61\%$, moderate-quality evidence) but had higher rates of clinical pregnancy (OR 1.93, 95% CI 1.42 to 2.64, 9 studies, 1027 women, $I^2 = 43\%$, moderate-quality evidence), ovulation (OR 2.55, 95% CI 1.81 to 3.59, 14 studies, 701 women, $I^2 = 58\%$, moderate-quality evidence) and menstrual frequency (OR 1.72, 95% CI 1.14 to 2.61, 7 studies, 427 women, $I^2 = 54\%$, low-quality evidence). There was no clear evidence of a difference in miscarriage rates (OR 1.08, 95% CI 0.50 to 2.35, 4 studies, 748 women, $I^2 = 0\%$, low-quality evidence). *Metformin plus clomiphene citrate versus clomiphene citrate alone:*

There was no conclusive evidence of a difference between the groups in live birth rates (OR 1.21, 95% CI 0.92 to 1.59, 9 studies, 1079 women, $I^2 = 20\%$, low-quality evidence), but gastrointestinal side effects were more common with combined therapy (OR 3.97, 95% CI 2.59 to 6.08, 3 studies, 591 women, $I^2 = 47\%$, moderate-quality evidence). However, the combined therapy group had higher rates of clinical pregnancy (OR 1.59, 95% CI 1.27 to 1.99, 16 studies, 1529 women, $I^2 = 33\%$, moderate-quality evidence) and ovulation (OR 1.57, 95% CI 1.28 to 1.92, 21 studies, 1624 women, $I^2 = 64\%$, moderate-quality evidence). There was a statistically significant difference in miscarriage rate per woman, with higher rates in the combined therapy group (OR 1.59, 95% CI 1.03 to 2.46, 9 studies, 1096 women, $I^2 = 0\%$, low-quality evidence) but this is of uncertain clinical significance due to low-quality evidence, and no clear difference between groups when we analysed miscarriage per pregnancy (OR 1.30, 95% CI 0.80 to 2.12, 8 studies; 400 pregnancies, $I^2 = 0\%$, low-quality evidence).

Metformin versus clomiphene citrate:

When all studies were combined, findings for live birth were inconclusive and inconsistent (OR 0.71, 95% CI 0.49 to 1.01, 5 studies, 741 women, $I^2 = 86\%$, very low-quality evidence). In subgroup analysis by obesity status, obese women had a lower birth rate in the metformin group (OR 0.30, 95% CI 0.17 to 0.52, 2 studies, 500 women, $I^2 = 0\%$, very low-quality evidence), while data from the non-obese group showed a possible benefit from metformin, with high heterogeneity (OR 1.71, 95% CI 1.00 to 2.94, 3 studies, 241 women, $I^2 = 78\%$, very low-quality evidence). Similarly, among obese women taking metformin there were lower rates of clinical pregnancy (OR 0.34, 95% CI 0.21 to 0.55, 2 studies, 500 women, $I^2 = 0\%$, very low-quality evidence) and ovulation (OR 0.29, 95% CI 0.20 to 0.43 2 studies, 500 women, $I^2 = 0\%$, low-quality evidence) while among non-obese women, the metformin group had more pregnancies (OR 1.56, 95% CI 1.05 to 2.33, 5 studies, 490 women, $I^2 = 41\%$, very low-quality evidence) and no clear difference in ovulation rates (OR 0.81, 95% CI 0.51 to 1.28, 4 studies, 312 women, low-quality evidence, $I^2=0\%$). There was no clear evidence of a difference in miscarriage rates (overall: OR 0.92, 95% CI 0.50 to 1.67, 5 studies, 741 women, $I^2 = 52\%$, very low-quality evidence).

Conclusions: Our updated review suggests that metformin alone may be beneficial over placebo for live birth, although the evidence quality was low. When metformin was compared with clomiphene citrate, data for live birth were inconclusive, and our findings were limited by lack of evidence. Results differed by body mass index (BMI), emphasising the importance of stratifying results by BMI. An improvement in clinical pregnancy and ovulation suggests that clomiphene citrate remains preferable to metformin for ovulation induction in obese women with PCOS. An improved clinical pregnancy and ovulation rate with metformin and clomiphene citrate versus clomiphene citrate alone suggests that combined therapy may be useful although we do not know whether this translates into increased live births. Women taking metformin alone or with combined therapy should be advised that

there is no evidence of increased miscarriages, but gastrointestinal side effects are more likely.

ULTRASOUND FETAL WEIGHT ESTIMATION DOES MORE HARM THAN GOOD

Basky Thilaganathan

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Fetal size currently serves as a common clinical proxy for placental dysfunction, but the issue of which fetal biometry chart to use continues to be a vexatious topic. The majority of stillbirths at term are not small for gestational age (SGA), questioning health policies focussed at detection SGA at term and the need for more 'accurate' fetal growth charts. Furthermore, both fetal size customisation and fetal growth velocity assessment have not been shown to improve detection of compromised pregnancies. Placental dysfunction is associated with both fetal smallness due to intrauterine malnutrition and fetal compromise from respiratory hypoxemia. Differing fetal nutritional and respiratory demands with advancing gestation support emerging data which consistently and convincingly show that fetal arterial redistribution on Doppler evaluation is more strongly associated with perinatal death at term than fetal size. A greater emphasis on properly conducted and powered trials of fetal wellbeing at term are now desperately required.

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INCREASED MISCARRIAGE OF EUPLOID PREGNANCIES IN OBESE WOMEN UNDERGOING CRYOPRESERVED EMBRYO TRANSFER

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Obesity is known to be associated with an increased risk of miscarriage after natural and assisted conception. Although most sporadic miscarriages are caused by genetic abnormalities, it is presently uncertain if genetics is also the underlying mechanism leading to increased pregnancy loss seen in obese women. Karyotyping of the products of conception suggests a reduced rate of fetal aneuploidy in miscarriages from obese compared with lean individuals. Karyotype analysis, however, is prone to false negative results because of inadvertent culture of maternal rather than fetal tissue. Therefore, to better analyse the effect of the genetic status on obesity-related miscarriage, we retrospectively analysed the outcomes 125 consecutive cryopreserved embryo transfer cycles resulting in a pregnancy after screening for genetic normality using comparative genomic hybridization. Lean individuals (body mass index 18.5–24.9 kg/m²) had a significantly lower rate of miscarriages (14.2%) than overweight (29.1%) or obese (41.9%) women ($P = 0.001$); this relationship remained significant ($P = 0.023$) even after adjusting for relevant confounders, e.g. maternal age, cause of infertility, number of previous IVF cycles, type of frozen embryo transfer cycle or past obstetric history. These results support a non-genetic cause for obesity-related miscarriage.



SELECTIVE OUTCOME REPORTING AND SPONSORSHIP IN RANDOMIZED CONTROLLED TRIALS IN IVF AND ICSI

Fulco van der Veen, *Netherlands*

The practice of decent medicine depends to a large extent on decent and high quality clinical research. The cornerstone of clinical research is the randomized clinical trial. Slowly but surely the methodology to perform a high quality trial has crystallized as well as the ethical requirements to design and start a trial. High quality implies robust internal validity, which can only be achieved if the trial is free from bias, defined as systematic errors that favour one outcome over the other. Potential sources of bias may be classified into selection bias (the selection and randomization of patients), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data caused by withdrawals) and reporting bias, caused by selective outcome reporting. Selective outcome reporting occurs if some outcomes are reported while others are not. This may be due to choosing a surrogate outcome instead of a clinically relevant one, or to not reporting pre-specified outcomes while outcomes that were not pre-specified are reported, without being declared as novel. This is an extremely common problem that distorts the evidence we use to make real-world clinical decisions as these outcomes are prone to be the result of chance alone. An additional problem is that results of trials using different outcome measures cannot be compared. Theoretically, Reproductive Medicine is especially susceptible to selective outcome reporting since there are many primary outcome measures to choose from – hormone levels, follicle development, number and quality of oocytes, fertilization rates, number and quality of embryos, endometrial thickness, biochemical pregnancy, clinical pregnancy, ongoing pregnancy, live birth, miscarriage, ectopic pregnancy, singleton pregnancy, multiple pregnancy, ovarian hyperstimulation syndrome etc. and many of these might not be the most relevant ones for clinical research. Also, there are many financial interests in the IVF industry and sponsorship by commercial parties is known to negatively influence valid interpretation of trial results by more often reporting on outcomes favourable to the sponsor's products. Data on selective outcome reporting and whether this is related to sponsorship in RCTs on IVF and ICSI are at present unknown. We here present data based on a systematic review of 415 identified RCTs in couples undergoing IVF and ICSI, performed between 2009 and 2014. Of the 415 RCTs, we excluded 235 (57%) for our primary analysis, because the sponsorship was not reported. Of the 180 RCTs included in the analysis, 7 trials did not report on any primary outcome measure and 107 of the remaining 173 trials (62%) reported on surrogate primary outcome measures like hormone levels or the number of oocytes retrieved. Of the 114 registered trials, 21 trials (18%) provided primary outcomes in their manuscript that were different from those in the trial registry. We found no association between selective outcome reporting and sponsorship. Additional analyses including the trials that had not reported sponsorship showed identical outcomes as in our primary analysis. Our findings show that the CONSORT statement, initiated to improve the quality of randomized clinical trials by lowering the chance of bias, is poorly adhered to in IVF/ICSI studies, and that the use of surrogate outcomes is highly prevalent, thereby obstructing insight into clinical outcomes that do matter. An effort to improve reporting is being done by the COMPare (CEBM Outcome Monitoring Project) team. This team is monitoring clinical trials for switched outcomes. Through increased awareness of misreported outcomes, individual accountability, and feedback for specific journals, they hope to fix the ongoing problem of selective outcome reporting.

BIOMARKERS FOR PRETERM BIRTH: VAGINAL CYTOKINES AND LACTOBACILLUS SPECIES

Gary Ventolini, *USA*

Worldwide, the most important cause of neonatal severity morbidity, disability and mortality (approximately 35% deaths) is preterm birth (PTB). PTB (less than 37 weeks' gestation) also represents a significant social and economic problem. PTB affects 500,000 or 1 of 9 infants born in USA. African American (AA) women have more than 1.5 times risk of PTB (16.8% vs. 10.5%) and 2 times risk of PTB at less than 32 weeks' gestation than Caucasian women. Although only less than 1/2 of the black-white disparity could be explained by socioeconomic status and other risk factors for PTB: mother age (less than 20 or more than 35 y/o), sexually transmitted infections (STI), underweight, obesity, chronic health conditions, short inter-pregnancy intervals, and tobacco/substance use. Maternal and/or fetal inflammation play a role in some PTB. Therefore, inflammation biomarkers might help to identify women at greater risk. Several studies have suggested the role of cytokines in the vaginal flora in the induction of PTB. To better understand these uncharacteristic changes that lead to preterm labor and PTB, it is important to first understand the cytokine alterations in the vaginal flora. The vaginal tract is home to more than 50 microbial non-pathogenic species. The vaginal microbiome (VM) varies widely and influences risk for PTB. Healthy VM plays a role preventing BV, STI, urinary tract infections, and HIV. Protection is attributed to *Lactobacillus* spp. and their competitive exclusion to pathogenic species. Bacterial vaginosis (BV) is characterized by a reduction in *Lactobacillus* spp. The Center for Disease Control in the USA estimates that 30% of women have BV surpassing 60% for AA women. BV is also associated with increased risks: STI, PTB among AA women. BV is a risk factor for PTB although a systematic review found no reduction in PTB risk after eradication of BV. Recently, it was published that VM from white, AA, Hispanic, and Asian women are clustering microbial communities into five groups. *Lactobacillus* spp. predominant in four and each microbial group and vaginal pH vary by ethnicity. Also, vaginal communities in which *Lactobacillus* spp. are not dominant are more common in AA (33%) than Caucasian (7%) women. Therefore, fluctuating levels of protective vaginal microbiota may explain racial disparities in BV and STD. Pregnant women have a significant reduction in taxonomic diversity as pregnancy progresses. Among Caucasian women greater diversity of the vaginal microbiome was found for those with term compared with PTB. We prospectively studied to quantify in consecutive low risk primigravidas vaginal pro-inflammatory cytokines and *Lactobacillus* spp. present. In our population, PTB primigravidas had significant vaginal prevalence of *L. iners* and cytokines: IL-6, IL-13, G-CSF and IFN- γ compared to patients who birthed term. IL-6 has been previously described, however, IL-13, G-CSF and IFN- γ are newly exposed.

MICROBIOME IN MENOPAUSE OR IN RELATION TO HORMONE LEVELS

Gary Ventolini, *USA*

The vaginal microbiome composition changes throughout a woman's lifetime from birth, through puberty, reproductive age and menopause. In early childhood we observe a dominance of Anaerobes, Diphtheroids, Coag-Negative Staph and *E. coli*. This condition is radically changed after menarche when *Lactobacillus* spp. colonize the vagina. At this point in time, the vaginal epithelium becoming estrogen embedded, proliferate, mature and accumulate glycogen which is nutritionally required by *Lactobacillus* spp. maintenance. New data regarding the role of human α -amylase which catabolizes glycogen into smaller polymers (maltose and maltotriose) is going to be talk over. In the post-menopausal period with the natural or provoked hormonal

decrease in ovarian estrogen production and circulating hormone levels, the vagina experiences the reduction of micro-anatomical features in vaginal epithelial cells available for *Lactobacillus* spp. nourishment. Therefore, it is now known that vaginal microbiome in menopause may well have a profound effect on vulvovaginal atrophy, vaginal dryness, sexual health, genitourinary symptoms and quality of life. We will be also discussing in great detail, the pathophysiology of microbiome in menopause, and in relation to hormonal level changes. Additionally, we will converse alterations associated with menopausal symptoms, and how hormone replacement therapy influences the vaginal microbiome dominance of *Lactobacillus* spp. homeostasis and menopausal symptoms themselves. We will review possible utilization of oral and vaginal probiotics to reestablish vaginal homeostasis after menopause. Moreover, we will explore further bacterial and nonbacterial therapeutics that could influence, modulate or restore vaginal homeostasis. Finally, recent published new information is going to be assessed regarding what vaginal normality means. This highpoints the necessity for more in-depth functional understanding of the interaction between the vaginal microbiome and host physiology, reproduction, defense and well-being. Please, join us in this journey to microbiome in menopause or in relation to hormone levels.

PHYSICAL CONCEPTS OF THE APPLICATION OF THE LASERS IN GYNECOLOGY AND THE TREATMENT OF VAGINAL RELAXATION SYNDROME

Zdenko Vizintin

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Objective: The aim of this paper is to present an update of the novel laser technology utilizing Erbium YAG laser for various minimally invasive non-surgical procedures in gynecology. Non-ablative, thermal-only Smooth mode erbium 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. This erbium laser technology was initially used for treatments of vaginal relaxation syndrome (VRS), but later got its role also in treatments of stress urinary incontinence (SUI), pelvic organ prolapse (POP) and genitourinary syndrome of menopause (GSM). **Methods:** In the period from 2010 to 2018 quite some clinical studies covering Vaginal Relaxation Syndrome (or Vaginal Laxity) were conducted with an aim to prove the efficacy and safety of this novel technology. An overview is presented of the results of these studies where several objective as well as subjective assessment tools were used. **Results:** Thirteen studies (having in total 572 patients) reported about the erbium laser treatment of VRS and measurements of its efficacy and safety. The tools used were dimensional measurements using wooden measurement stick (for longitudinal) and MRI images (for cross section dimensions), perineometric pressure changes and questionnaires: PISQ12, FSFI and 3 and 4 grades Likert scales. All used tools showed significant improvement of measured values. The treatment discomfort was very low (the maximum score was 3 on a 10-grade scale) and a large majority of the patients assessed their improvement very positively. There were no adverse effects of these treatments reported. **Conclusions:** The results have shown that Smooth mode erbium laser seems to be an effective and safe method for treating vaginal relaxation syndrome as well as some other gynecological indications as are SUI, GSM and POP.

PREMATURE OVARIAN INSUFFICIENCY- POI: ADVANCES IN DIAGNOSIS AND MANAGEMENT

Lisa Webber, UK

Premature ovarian insufficiency is a distressing condition that affects 1% of women. Iatrogenic POI is increasing as more successful treatments for cancer lead to more young survivors living with the reproductive consequences. In addition, chemotherapies, especially for stem cell transplants, are being increasingly used for benign chronic conditions. POI affects fertility, sexual relationships, bone health, cardiovascular health, quality of life and even life expectancy. It is not a difficult diagnosis to make, although it is a difficult one to deliver and to receive. For many years, management of the condition was limited to prescribing hormone replacement and offering egg donation. Whilst those basic principles have not changed, women with POI need support and engagement, with their changing needs being addressed in a collaborative and sympathetic way. Managed health care/commissioning restrictions can get in the way of providing holistic care to this group. At the end of 2015, the European Society for Human Reproduction & Embryology (ESHRE) published a comprehensive guideline on the diagnosis and management of POI with the aim of improving care and also to provide evidence-based information to affected women and their careers. Key points in the diagnosis of this condition will be discussed and the management challenges of women with POI who have co-existing medical problems will be explored.

RADIO FREQUENCY ABLATION, NONSURGICAL AND MINIMALLY INVASIVE THERAPIES FOR THE PRESERVATION OF THE FIBROID UTERUS

Jessica Ybanez-Morano, USA

Uterine fibroids (leiomyomas) are the most common benign pelvic tumors in reproductive age women, which occur in approximately 20-40% of women in this age group. The current management options include medical (hormonal and nonhormonal), nonsurgical and minimally invasive therapies (uterine artery embolization, image-guided thermal ablation, magnetic resonance-guided focused ultrasound surgery, radiofrequency ablation, and percutaneous microwave ablation) and surgical (myomectomy and hysterectomy). Laparoscopic, ultra-sound guided radiofrequency ablation (RFA) is a uterine sparing procedure for uterine fibroids. RFA was developed to provide women with a minimally invasive option for fibroid treatment that is safe, effective and uterine conservation. It is effective in treating fibroids of various sizes and number. RFA does not require uterine incisions and provide decreased myoma symptoms, improved quality of life. Recovery time is brief. It is important to understand the procedure, gain appropriate training and improve surgical abilities to optimize clinical outcomes.

WHAT IS NEW IN HIV

Mark Yudin, Canada

With recent advances in care, individuals living with HIV are expected to have similar life expectancy rates as their HIV-negative peers. With improvements in health and survival rates, pregnancy and family planning have emerged as important issues for this community. The management of HIV in pregnancy can be complex. Similarly, there are many issues that need to be considered when planning pregnancies in the context of HIV. When one or both prospective parents is living with HIV, there are various options to achieve pregnancy. This presentation will review the issues related to pregnancy planning and will present a summary of the recently updated Canadian HIV Pregnancy Planning Guidelines. It will also review recently published data relating to horizontal HIV transmission during family planning.



ORAL PRESENTATION ABSTRACTS

OP1-101

INTRAUTERINE ADMINISTRATION OF HUMAN CHORIONIC GONADOTROPIN (HCG) FOR SUBFERTILE WOMEN UNDERGOING ASSISTED REPRODUCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Problem statement: Most women undergoing assisted reproduction treatment will reach the stage of embryo transfer (ET), but the proportion of embryos that successfully implant following ET has remained small since the mid-1990s. Intrauterine administration of human chorionic gonadotropin (hCG) around the time of ET is a novel approach that has recently been suggested to improve the outcomes of assisted reproduction. The objective of this study was to investigate whether the intrauterine administration of hCG (IC-hCG) around the time of ET improves the clinical outcomes in subfertile women undergoing assisted reproduction.

Methods: Cochrane methods were used to search the standard medical databases (9 January 2018) and to meta-analyse randomized controlled trials (RCTs) evaluating the use of IC-hCG around the time of ET. **Results:** Seventeen RCTs including 4751 subfertile women undergoing assisted reproduction were meta-analysed. Women undergoing cleavage-stage ETs with an IC-hCG dose of 500 IU or greater had a higher live birth rate (risk ratio (RR) 1.57, 95% confidence interval (CI) 1.32 to 1.87, three RCTs, 914 participants) and a higher clinical pregnancy rate (RR 1.49, 95% CI 1.32 to 1.68, twelve RCTs, 2186 participants) compared to women having cleavage-stage ETs without IC-hCG. Women undergoing blastocyst-stage ETs with an IC-hCG dose of 500 IU or greater had a similar live birth rate (RR 0.92, 95% CI 0.80 to 1.04, two RCTs, 1666 participants) and a similar clinical pregnancy rate (RR 0.99, 95% CI 0.85 to 1.15, four RCTs, 2091 participants) compared to women having blastocyst-stage ETs without IC-hCG. There was no evidence that miscarriage was influenced by intrauterine hCG administration (RR 1.04, 95% CI 0.81 to 1.35, 11 RCTs, 3927 participants). **Conclusions:** The improved pregnancy outcome for cleavage-stage transfers using an IC-hCG dose of 500 IU or greater is clinically important. Given the strength of the evidence we believe that patients will benefit from this intervention. However, the current evidence for IC-hCG treatment does not support its use for blastocyst transfers.

OP1-102

THE RELATIONSHIP BETWEEN THE ELEVATED PREOVULATORY AND POSTOVULATORY PROGESTERONE SERUM CONCENTRATION AND THE OUTCOME OF IN VITRO FERTILIZATION

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Problem statement: The influence of elevated preovulatory and postovulatory progesterone (P₄) on the outcome of in vitro fertilization (IVF) has been in the focus of many discussions in contemporary reproductive endocrinology. Numerous studies have found the adverse effect of elevated preovulatory P₄ on the outcome of IVF, while other studies failed to do so. Hence, there

are no clearly established strategies in the treatment of patients with elevated preovulatory P₄. The outcome of IVF procedures among normal and elevated preovulatory P₄ and postovulatory P₄ patients has been analyzed in this study. **Methods:** This is a prospective cohort study which included 400 patients (300 controls with P₄<4,77 nmol/l, 100 in the study group with P₄>4,77 nmol/l-85 normal responders, 15 high responders). Exclusion criteria for the study were: age 37, patients with high P₄ on 2nd, 3rd and 4th cycle day and poor responders. Data and patients' blood samples were collected during the 3-year period (2015-2017) at the Department of Obstetrics and Gynecology, University Hospital Center Zagreb. Results were analyzed using SPSS program version 23.0. The statistical significance was set at a p value of <0,01. **Results:** The mean number of retrieved oocytes in the control group was 7 (5-11) and 14 (10-17) in the study group while the mean number of fertilized oocytes was 5 (3-8) and 9,5 (7-12) respectively, p<0,001. No difference has been found between the groups regarding implantation rate (34,3% vs 36%, $\chi^2=0,092$; p=0,762) and clinical pregnancy rate (26% vs 32%, $\chi^2=1,354$; p=0,245). Implantation and clinical pregnancy rate among normal responders were 35,3% and 30,6%, among high responders both parameters were 40%. High sensitivity (86,21%, 95%CI 81,7-90,0%) and low specificity (23,64%, 95%CI 16,1-32,7%) of P₄ on 5th postovulatory day has been found at P₄ value of $\leq 425,7$ nmol/l among all the patients regarding the IVF outcome. **Conclusion:** This study found no relationship between the elevated preovulatory P₄ and the adverse IVF outcome, while postovulatory P₄ $\leq 425,7$ nmol/l seems to have an adverse effect on IVF outcome. It is preferable to perform FET with elevated preovulatory P₄ as the improved implantation and clinical pregnancy rate has been recorded.

The authors have nothing to disclose.

OP1-103

ROLE OF PROGESTERONE LEVEL ON DAY OF HCG INJECTION IN IVF CYCLES ON CLINICAL PREGNANCY RATE

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Problem Statement: Premature progesterone rise (PPR) has long been implicated as contributing to implantation failure. Despite the use of gonadotropin-releasing hormone (GnRH) analogues, subtle increases in serum progesterone (P₄) levels beyond a threshold progesterone concentration are observed on the day of trigger in controlled ovarian hyperstimulation cycles. The purpose of the study was to evaluate the incidence of premature progesterone rise on day of hCG trigger in conventional IVF/ICSI cycles and its impact on clinical pregnancy rate. **Methods:** 235 patients undergoing conventional IVF/IVF-ICSI by fresh embryo transfer cycles from January 2016 to December 2016 at infertility unit of a tertiary care hospital were prospectively analyzed. Patients included in the study were subjected to GnRH agonist long/antagonist protocol. Ovulation induction was given with rFSH and/or HMG in both the protocols. The cutoff for defining PPR was progesterone ≥ 1.5 ng/ml; and an analysis of impact of progesterone on day of hCG trigger on clinical pregnancy rate was performed. **Result:** The overall clinical pregnancy rate per embryo transfer was 30.6%. The clinical pregnancy rate in the patients with P₄ ≤ 1.5 ng/ml was significantly higher than those with elevated levels, P₄ ≥ 1.5 ng/ml (33.3% vs. 12.9%; P = 0.037). **Conclusion:** The measurement of serum progesterone levels in the late follicular phase is important in COH cycles for IVF/ICSI, with higher progesterone levels on day of trigger leading to a significantly adverse outcome. Factors implicated in PPR were the type of protocol, type and total dose of gonadotropin given, E₂ levels on the day of trigger, and the number of intermediate follicles recruited.

OP1-104

THE ASSOCIATION BETWEEN CIRCULATING NEUREGULIN 4 LEVELS, METABOLIC, ATEROGENIC AND AMH PROFILE OF POLYCYSTIC OVARY SYNDROME

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Problem Statement: Polycystic ovary syndrome (PCOS) is a metabolic disorder associated with obesity and adipose tissue disturbances. Neuregulin 4 (NGR4) is secreted from adipose tissue and its function to regulate energy metabolism. This current study was designed to assess NGR4 levels in normal weight and obese women with polycystic ovary syndrome (PCOS) and to assess their relationship with anti-Mullerian hormone (AMH) levels, atherogenic profile and metabolic parameters. **Methods:** This prospective cross-sectional study included 148 women and divided into four groups; The study group was composed of 40 normal weight and 39 obese women with PCOS diagnosed based on the Rotterdam criteria; 38 normal weight and 31 obese age matched non-hyperandrogenemic women with regular menstrual cycle. Serum Neuregulin 4 homeostasis model assessment of insulin resistance (HOMA-IR) and AMH levels were evaluated. Univariate and multivariate analyses were performed between Neuregulin 4 levels and AMH levels, metabolic and atherogenic parameters. **Results:** Serum NGR4 values were elevated in the normal weight PCOS subgroup than in the control group. Moreover, serum NGR4 levels were higher in the obese PCOS subgroup than in normal weight PCOS and obese control subgroups. (p<0.01) In the univariate analyses revealed that Body mass index (BMI), Waist/Hip oranı, TG, HsCRP, Glucose, Insulin, HOMA-IR, AMH ve DHEAS positively correlated with NGR4. In the multivariate analyses BMI is positively predicted NGR4 levels. **Conclusion:** Metabolic abnormalities in PCOS are related to obesity. Adipose tissue related molecules NGR4 may play key role in the pathophysiology of the PCOS. **Key words:** Neuregulin 4 (NGR4), Obesity, Polycystic ovary syndrome (PCOS)

OP1-105

IMPACT OF ETHNICITY ON FRESH AND FROZEN EMBRYO TRANSFER OUTCOMES

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Problem statement: There is evidence that ethnicity affects in-vitro fertilisation (IVF) outcomes, with women of South Asian and Afro-Caribbean ethnicities having lower live birth rates. However, most data focusses on fresh embryo transfers and there is limited literature regarding the impact of ethnicity on frozen embryo transfers. **Methods:** The subject of assessing ethnic variation precludes a clinical trial and therefore a cohort study framework was used. We performed a retrospective analysis of outcomes following fresh and frozen embryo transfers performed at our unit between 2010 and 2016. Only the first fresh embryo transfer and first frozen embryo transfer was analysed per woman having IVF and so the per-cycle and per-woman results are similar. We adjusted for confounders including age, number of oocytes retrieved and number of embryos transferred when comparing the live birth rates per embryo transfer. **Results:** We compared fresh embryo transfer outcomes for 5876 Caucasian, 1071 South Asian and 114 Afro-Caribbean women. South Asian women had a lower live birth rate than Caucasian women (26% vs 32%, aOR 0.622, 95% CI 0.533 to 0.725, p<0.001). Afro-Caribbean women also had a lower live birth rate as compared to Caucasian women (21% vs 32%, aOR 0.528, 95% CI 0.332 to 0.839, p=0.007). We compared

frozen embryo transfer outcomes for 1418 Caucasian, 273 South Asian and 31 Afro-Caribbean women. The live birth rates per frozen embryo transfer were not significantly different between South Asian and Caucasian women (26% vs 27%, aOR 0.890, 95% CI 0.661 to 1.200, p=0.445) and between Afro-Caribbean and Caucasian women (29% vs 27%, aOR 0.983, 95% CI 0.447 to 2.162, p=0.966). **Conclusion:** These results appear to indicate that ethnicity had a greater impact on fresh embryo transfer than frozen embryo transfer outcomes. There is evidence that the steroidogenic profiles during fresh IVF cycles are different between ethnicities, with South Asian and Afro-Caribbean women having higher peak estradiol levels. In addition, South Asian women appear to have a higher prevalence of premature progesterone rise before ovulation trigger. These results indicate that the impact of ethnicity may be primarily endometrial (in a fresh embryo transfer environment) than embryonic.

OP1-106

ADVANCED MATERNAL AGE AND IVF RESULTS AFTER PREIMPLANTATION GENETIC SCREENING

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Problem statement. Patients with advanced maternal age (AMA) have poor IVF outcome and high miscarriage rate, which suggested the necessity of preimplantation genetic screening (PGS). From the other hand new approaches to PGS, for example the method of next generation sequencing (NGS), increase the chances for the patients to get pregnancy. So the aim of this study was to investigate the results of PGS and IVF outcome in women over 39 years old and to compare the obtained results with the younger patients. **Methods.** This study was performed at Centre of Human Reproduction "Clinic of Professor Feskov" (Kharkov, Ukraine). Eighty three infertile couples participated in the study between January and December 2017. Two groups were formed taking into account the women age: 51 women up to 39 years old in Group 1; 32 women over 39 y.o. in Group 2. All the mentioned patients were subjected to in vitro fertilization-preimplantation genetic diagnosis (IVF-PGD) treatment. Blastocyst biopsy was performed on 5th and 6th days of the embryo development (fig. 1). Totally 313 preimplantation blastocysts were examined using the method of NGS. **Results.** The part of euploid blastocyst was significantly higher in patients from Group 1 (64.3% vs. 23.9%, $\chi^2 = 33.104$, P 0.01). The aneuploidies of chromosomes 1, 2, 4, 5, 7, 8, 16, 18, 21, 22, X and Y were detected in embryos as a result of PGD procedure. Totally 40 single embryo transfers (SETs) were done: 28 SETs for younger patients and 12 SETs for women with advanced maternal age. No difference in the pregnancy rates were found between the patients from both groups: 53.6 % vs. 41.6 % ($\chi^2 = 2.887$, P 0.05).



Conclusion. The obtained results witness that patients with higher maternal age had worse chances to get the euploid blastocyst in IVF cycle. From the other hand the choice of the embryo with balanced karyotype significantly increases chances to get pregnancy in advanced maternal age.

OP1-107

MTHFR SNPs CONSEQUENCES ON GAMETES AND EMBRYOS AFFECT EQUALLY MEN AND WOMEN FERTILITY AND CAN BE OVERCOME WITH TREATMENT: 5MTHF WITH ONE CARBON CYCLE SUPPORT (1-CC)

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Problem statement: Methylation is involved in imprinting and epigenesis during gametogenesis. MTHFR (methylene tetrahydrofolate reductase) is a crucial step in this process as it allows the formation of 5MTHF, which allows the recycling of Homocysteine, a cellular poison, inhibitor of methylation. MTHFR single nucleotides polymorphisms (SNPs) (677CT and/or A1298C) can severely reduce the enzymatic conversion and decrease the regeneration of methionine from homocysteine: this induces a block in the 1-CC and an accumulation of homocysteine. These SNPs affect gametogenesis (Dong), early embryogenesis (Enciso), trophoblast development (Serman; Dodig). In this study, we have determined the MTHFR SNPs background from couples having a long lasting infertility. Then, we tested the impact of an external supply of 5 MTHF, backed up with a support of the one carbon cycle (Impryl® or Tetrafolac®). **Methods:** In a group of 14 couples that had a total of 61 miscarriages (4.36 per couple) the MTHFR SNPs A1298C and C677T were tested. 2 of these couples had been counseled for oocyte donation; All the patients tested positive were counseled to take the treatment at least 3 months with protected intercourse. **Results:** The following distribution was observed: Men and women HTZ: 7 couples; Women HMZ, Man WT: 2 couples; Woman HMZ, man HTZ: 3 couples; Man HMZ, Woman HTZ: one couple. Both members HMZ: 1 couple. No combined SNP status was observed in this group. After treatment, 12 ongoing pregnancies (including 7 deliveries) have been observed, spontaneously or after ART. One pregnancy ends up with a miscarriage and one couple failed all the ART treatments so far. **Conclusions:** Both members of couples with RPLs should be tested for the 2 major MTHFR SNPs. This should be a mandatory screening (Servy), even before oocyte donation. The SNP carriers should be treated before conception, with 5MTHF associated with a support of the 1-CC.

OP1-201

THE ROLE OF ANTIBODIES TO STEROID HORMONES AND CHEMICAL CARCINOGEN BENZO[A]PYRENE IN WOMEN WITH ENDOMETRIOSIS

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Problem statement. Endometriosis is an estrogen dependent gynecologic disease with lasting implications for many women's fertility, somatic health, and overall quality of life. Growing evidence suggests that endocrine disrupting chemicals (EDCs) may be etiologically involved in the development and severity of disease [Smarr MM, 2016]. A growing body of evidence suggests that endocrine-disrupting chemicals (EDCs) contribute to female reproductive disorders [Hunt A., 2016]. **Objective** of this study was to determine antibodies of immunoglobulin (Ig) classes A and G to

estradiol (E2), progesterone (P), benzo[a]pyrene (Bp) and their ratios in women with endometriosis. **Methods.** It was a retrospective, case-control study. This study included 200 women. Group I consisted of 100 women with histologically verified of endometriosis. Group II consisted of 100 women with tubal infertility. All patients underwent immunological examination of serum, steroid hormone levels (progesterone, estradiol), antibodies to them and benzo[a]pyrene were determined. Immunoassay of IgA and IgG antibodies to progesterone, estradiol and benzo[a]pyrene was performed with non-competitive enzyme-linked immunosorbent assay (ELISA). ROC analysis was performed to reveal threshold values of antibody levels. **The results** of the study showed that women with endometriosis had statistically significant higher levels of IgG-class antibodies to progesterone (OR=7.9 (95% CI, 3.9-15.9), $\chi^2=35.9$, p0.0001), estradiol (OR=4.5 (95% CI, 2.4-8.5), $\chi^2=22.1$, p0.0001) and benzo[a]pyrene (OR=27.3 (95% CI, 2.9-11.0), $\chi^2=27.3$, P0.0001) compared with women from Group II. As well as statistically significant, higher levels of IgA-class antibodies to progesterone (OR=2.4 (95% CI, 1.4-4.4), $\chi^2= 8.4$, P=0.004), estradiol (OR=3.3 (95% CI, 1.8-6.0), $\chi^2=14.4$, P=0.0001) and benzo[a]pyrene (OR=13.6 (95% CI, 1.7-5.5), $\chi^2=13.6$, P=0.0002). **Conclusion.** Thus, immunological features of patients with endometriosis were elevated levels of antibodies IgA and IgG to progesterone, estradiol and benzo[a]pyrene. The obtained data can be regarded as risk factors for the development of endometriosis and promising markers for the creation of a disease prediction system. Determination of antibodies and their relationship to estradiol, progesterone and benzo[a]pyrene probably can be used to predict endometriosis.

OP1-202

ADENOMYOSIS: ROLE OF STEM CELLS MARKERS IN THE PATHOGENESIS.

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Problem statement: Adenomyosis is a common gynecologic disorder affecting 8–62 % of women of reproductive age. According to one of the theories of adenomyosis development, hematopoietic stem cells can differentiate into endometrioid tissue at ectopic sites in myometrium. Endometrial stem cells have a long proliferating potential and produce glandular-like and stroma-like cells. Abnormal proliferation of stem endometrial cells can be involved in the pathogenesis of adenomyosis, as well as endometriosis and endometrial cancer. **Methods:** 150 women who underwent surgery for adenomyosis between 2014 and 2016, were enrolled in the study. 40 tissue samples of adenomyosis and endometrium for immunohistochemical study were obtained. The investigation of the molecularbiological features of the foci of adenomyosis and to determine their connection with progenitor and stem cells was conducted with comparison of molecular biological features of eutopic endometrium and adenomyosis foci by studying the expression of markers of stem cells and progenitor cells (COX-2, Oct-4, CD34, Musashi-1). **Results:** Immunohistochemical analysis of endometrial tissue and adenomyosis showed a positive reaction with Musashi-1 was in both nuclei and in the cytoplasm of glandular and stromal cells. The maximum values were found in the nuclei of epithelial cells, where they exceeded the analogous phase of secretion by 35%. The cytoplasmic level of expression of Musashi-1 in proliferating epithelium was 21.7% higher than the values of the secretion phase. According to the quantitative analysis of the intensity of the reaction on COX-2, it was established that in the tissue of normal endometrium the highest level of expression was observed in epithelial cells during the proliferation phase. Positive immunohistochemical reaction with OCT4 was observed in the



nuclei of epithelial and stromal cells. In the observations of nodular adenomyosis, such OCT4 + epithelial and stromal cells were more by 67.7% and 41.3%, respectively, than in the eutopic endometrium of the proliferation phase. In areas of diffuse adenomyosis, their number exceeded the same parameters by 123.2% and 90.4%, respectively (p 0.05). **Conclusion:** Expression of stem cells markers in adenomyosis is observed and they may be involved in the pathogenesis and pathophysiology of adenomyosis

OP1-203

ECTOPIC PREGNANCIES IN UNUSUAL LOCATIONS

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Introduction: A cornual ectopic occurs when the conceptus implants in the interstitial part of the fallopian tube. It is one of the rarest forms of ectopic pregnancies, accounting for about 1.1 to 6.3% of all ectopic pregnancies and is associated with higher morbidity. On the other hand, a cesarean scar ectopic occurs when the conceptus implants in the scar of a previous cesarean through a microscopic dehiscence tract. It constitutes about 6.1% of all ectopic pregnancies in women who had a previous cesarean and has an incidence of 1:1800. **Methods:** In this case series we present four cases. The first two involve patients who were diagnosed with a cornual ectopic. Both had had an ectopic pregnancy which was treated with a salpingectomy within the previous two years. The first case was diagnosed during surgery whilst the other patient was diagnosed preoperatively by ultrasound, with both patients receiving surgical management. The other patients who were diagnosed with a Cesarean scar ectopic were both multigravidas with a history of cesarean deliveries. Both had medical management of miscarriage followed by surgical evacuation, during which a Cesarean scar ectopic was confirmed and the products of conception were removed during a subsequent laparotomy with oversuturing of the defect in the uterus to secure hemostasis. **Results:** All cases, whether diagnosed preoperatively by ultrasound or intraoperatively, were successfully managed and the patients involved were discharged from hospital after a few days. **Conclusion:** Cornual ectopics are amongst the rarest forms of ectopic pregnancies and as such are difficult to diagnose. Unlike tubal pregnancies, such ectopic pregnancies are more likely to rupture early in the gestation, as happened in these two cases. Surgical management is ideal when the patient is unstable as it gives the best chance of survival. With regards to cesarean scar ectopic pregnancies, consensus on the best management has not been reached yet and to date different treatment modalities have been successful. It is worth noting that the incidence of such ectopic pregnancies is on the rise and could be due to the increasing trend towards delivery by cesarean section.

OP1-204

HOW VAGINAL MICROBIOTA'S RE-ESTABLISHMENT CAN REDUCE SEXUALLY TRANSMITTED DISEASES: AN OBSERVATIONAL STUDY ON 2010 PATIENTS

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Problem Statement: Human body is mostly made by trillions of microbes, identified as microbiome. The number of genes in all the microbes in one person's microbiome is 200 times the number of genes in the human genome, then some authors defined humans as "living colonies". Microbiome is fundamental in protecting against pathogens. Vaginal ecosystem, even with its own features, is related and deeply linked with other barrier systems of the body such as gut, urinary system and skin. Vaginal flora is essentially made by Lactobacilli and eubiosis is guaranteed by the balance

existing between good microbes and pathogens and by creating a protective "biofilm" needed to tackle infections and defend from diseases, same as happens in the gut. Changes in vaginal microflora creates a condition called "dysbiosis", causing a predominance of pathogens (pathobiosis). The aim of this study was to evaluate how Lactobacilli implementation can avoid vaginal flora modifications and coinfections. **Methods:** From January 2007 to December 2017 all women presenting to outpatient clinic of Sexually Transmitted Disease (STD) at Policlinico Umberto I, Sapienza University of Rome, were evaluated with bacterioscopic examination and investigated for possible coinfections, trying to identify correlations between different germs development in an altered ecosystem. In women with pathologic results a validated protocol of Lactobacilli administration based on Lactobacillus rhamnosus BMX54 was adopted (once a day for 15 days, twice a week for 15 days, and then once a week for 6 months). **Results:** Overall, 2010 patients were screened. Of those, 1210 patients (60%) presented alterations of vaginal microflora while 800 (40%) had normal results. In 645 patients with microflora alteration identified by bacterioscopic exam (mixed bacterial flora or bacterial vaginosis) a STD was detected. All those patients underwent a Lactobacilli implementation and significant improvement in infections control (p=0.001) and prevention of recurrences after 12 months was obtained (p=0.003). **Conclusion:** Often, slight alterations of vaginal microflora can promote good bacterial overgrowth but mainly might further coinfection with other pathogens, giving an higher predisposition to STD. But by re-establishing eubiosis in vaginal ecosystem, bacterial and viral predominance could be reduced, leading to a lower susceptibility to coinfections.

OP1-205

THE MODERN CATHOLIC CHURCH AND CONTRACEPTION – STARTING A DIALOGUE ABOUT RETHINKING THE CHURCH'S POSITION ON CONTRACEPTION

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Problem statement: The modern Catholic Church represents a body of 1.3 billion people who follow the Church's teachings given to them in the form of documents on different topics, including family issues, family planning, etc. The latest 2016 Apostolic Exhortation *Amoris Laetitia* confirmed the previous documents on the topic, confirming periodical abstinence as the only contraceptive method possible for Catholic Christians. This means that 1.3 billion people are forbidden to use modern contraception, which significantly contributes to the global epidemic of unintended pregnancies and their consequences and the spread of sexually transmitted infections. **Methods:** This report is based on the analysis of the latest 2016 Apostolic Exhortation *Amoris Laetitia* (as well as the previous papal encyclicals and documents) and on data from FIGO's Committee for Women's Health and Human Rights (2017 Newsletter – *Women's Health Challenges*), FIGO's presentation on *The Global Epidemic of Unintended Pregnancies*, and WHO's 2017 *Sheet on Family Planning and Contraception*. **Results:** Globally, nearly 41% of all pregnancies are unintended (some 86 million out of a total 208 million pregnancies a year). The percentage varies from continent to continent, the highest is in Latin America (58%). This epidemic results in consequences such as induced abortions (there are 56 million abortions a year globally) maternal mortality (globally 303,000 women die a year due to the pregnancy-related issues, two-thirds of these deaths happen in Sub-Saharan Africa). In both cases, i.e., Latin America and Sub-Saharan Africa, the Catholic Church prevails. Unintended pregnancies and their consequences are preventable if women are well informed about contraception and family planning services and if they are free to choose a contraceptive method based on their personal opinion, expectations, contraindications, etc.



Conclusion: Given the severity of gynecological problems and the number of adherents to the Catholic Church, international gynecological organizations need to initiate a dialogue with representatives of the Catholic Church about rethinking its position on contraception and family planning services, for the sake of improving the position and health of women, which will be followed by a decrease in maternal and infant mortality and morbidity, a decrease in induced abortions, and sexually transmitted infections.

OP1-206

PREVALENCE OF PELVIC FLOOR DYSFUNCTION SYMPTOMS IN REPRODUCTIVE AGE WOMEN

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Problem statement. The term 'pelvic floor disorders' (PFDs) refers to stress urinary incontinence, overactive bladder syndrome, pelvic organ prolapse and fecal incontinence. These disorders are prevalent in adult women. Childbirth is an important event in a woman's life. Vaginal childbirth is the most common mode of delivery and it has been associated with increased incidence of pelvic floor disorders later in life. [Memon U., 2013]. According to different studies, the rates of PFD symptoms varies from 19.7 to 77.2% [Walker GJ, 2011, Awwad J, 2012]. The prevalence of PFD symptoms in women of reproductive age is poorly understood.

Objective was to estimate frequency of pelvic floor dysfunction (PFD) symptoms in reproductive age women and their relationship with childbirth. **Methods.** 1637 women between the ages of 18 and 45 (mean age 30.8± 5.7 years old) who were questioned using the PFDI-20 questionnaire (Pelvic Floor Inventory Questionnaire) and the Female Sexual Function Index (FSFI). **Results.** The results of the study showed the PFD symptoms in almost half of reproductive age women: symptoms of POP were recorded in 46.6%, colorectal anal symptoms – in 43.3%, and urinary incontinence – in 49.7% of women. According to the FSFI questionnaire, the frequency of sexual disorders was 80.7%. The relationship between symptoms of PFD and childbirth was established: symptoms of POP ($\chi^2=92.96$, $p=0,0001$), colorectal anal symptoms ($\chi^2=132.22$, $p=0,0001$) and urinary symptoms ($\chi^2=123.68$, $p=0,0001$). The relationship of sexual disorders with the presence of childbirth was not established ($\chi^2=0.1005$, $p=0,751$). **Conclusion.** A high incidence of symptoms of pelvic floor dysfunction in women of reproductive age and its relationship to childbirth has been established, which requires the development of a set of measures to prevent these disorders in women in the postpartum period. **Conflict of interest.** The authors do not have a conflict of interest.

OP1-207

CONSERVATIVE TREATMENT OF CERVICAL ECTOPIC PREGNANCY: METHOTREXATE VS UTERINE ARTERY EMBOLIZATION

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Problem statement: Preserving fertility in patients with cervical ectopic pregnancy especially after IVF is serious problem in operative gynecology. **Methods:** Prospective and retrospective analysis enrolled 58 women with cervical pregnancies (ages 25–47 years) treated in Operative Gynecology department during 12 recent years. 33 of them underwent combined therapy with preoperative systemic methotrexate chemotherapy (early observations) and in 14 cases with chorion invasion into the cervix we used selective uterine artery embolization (SUAE) following with minimal invasive surgery (resectoscopy) for preserving fertility. Additional laparoscopic removal of ovarian teratoma was performed in one case. **Results:** Clinical protocol included

transvaginal ultrasound investigation with transducer for color Doppler mapping, MRI to visualize gestational sac, boundaries between the chorion and stroma of the cervix; assessment of the blood flow in the chorion, the evaluation of β -hCG in serum. In 55 cases diagnostic hysteroscopy and followed resectoscopic removal of the chorion and coagulation of the vessels were performed. The term of pregnancy on admission ranged from 5 to 9 weeks of gestation and the average term was $6,4 \pm 0,8$ weeks. Patients with cervical pregnancy received i/v methotrexate at an average of 50 mg/every 48 hours, 6 mg of leucovorin administered i/m after 28 hours after methotrexate injection. The total dose of administered methotrexate ranged from 200 to 300 mg and depended on the patient's body weight, week of gestation, level of β -hCG and intensity of chorion blood flow. Surgical procedure started at decreased level of β -hCG about 4000-7000 IU/l. SUAE on both sides applied in 12 cases through the right femoral approach and in 2 cases through the right radial artery. Hysterectomy was performed in 3 cases. The effectiveness of organ-sparing treatment of cervical pregnancy is 94,8%. **Conclusion:** The results of our study suggest that resectoscopic removing of embryo with previous cytostatic therapy with methotrexate allows to save fertility in young women with early cervical pregnancy. SUAE provides minimal operative blood loss, more shorter hospital stay and does not hurt reproductive function.

OP1-208

NEW THEORY OF NORMAL AND DEVIANT UTEROVAGINAL EMBRYOGENESIS

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Problem statement: Investigations of female genital development in early human embryos still poses many controversies, because it is difficult to assess early stages of an embryo. In the original Mullerian theory (1830): the paramesonephral ducts form the Fallopian tubes, uterus and vagina; the mesonephral ducts regress in female embryos. The new theory of embryonic genital morphogenesis based on systematic comparison of uterovaginal malformations with the literature review. **Methods:** Between 1998 and 2018, the 645 patients with various uterovaginal malformations and the 156 females with various disorders of sex development had been operated on at the National Research Center of Obstetrics Gynaecology and Perinatology after V Kulakov in Moscow, Russia. The anatomies of the uterovaginal malformations in these patients were diagnosed by ultrasound and MRI and then verified during laparoscopy. **Results:** Congenital malformations are defined as deviations from normal embryogenesis, each variant of them corresponds to the persistent developmental stages, such as: Mullerian ducts aplasia, fusion defects, persistence of the intermedial septum. Surgical treatment performed according of the anomalies type, the patient's symptoms and the concomitant gynecological pathology by laparoscopy and hysteroscopy, following histological investigation. The new method of functional (dynamic enhanced) MRI involved for estimation of uterine blood perfusion; which reduced up to ≥ 20 -32 % in most patients with septate uterus, affirming the hysteroresectoscopic metroplasty. More than 52% patients had concomitant pathology; endometriosis was still major factor of pain and infertility in 46% patients, same in symmetric (non-obstructive) and obstructive anomalies. The new theory is significantly different: ovary, ovarian and broad ligaments derive from the gonadal ridges, which are composed from primordial germ cells; Fallopian tubes and vagina completely develop from mesonephral ducts. The uterus develops in the area of intersection between the mesonephral ducts with gonadal ridges by the fusion of the two. **Conclusion:** The new insight of theory, that the ovarian germline epithelium, eutopic and ectopic endometrium are derive from the gonadal ridges from polypotential germ cells. It could be the key to understanding the enigmatic aetiologies of external and ovarian endometriosis, originating from primordial germ cells.



OP1-209

SUPPLEMENTATION OF GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR TO CULTURE MEDIUM MIGHT RECTIFY PREGNANCY RATES IN PATIENTS HAVING HISTORY OF FAILED IVF DUE TO EMBRYO DEVELOPMENT ARREST

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Problem statement: Does use of culture media including granulocyte-macrophage colony-stimulating factor (GM-CSF) rectify pregnancy in patients with history of recurrent cycle cancellation due to embryo development arrest? **Methods:** Between January-2016 and November-2017, a total of 49 patients were retrospectively identified from database of IVF Center, Hacettepe University in which culture media containing GM-CSF (Embryogen, Origio, Denmark) was preferred. Only patients with history of ≥ 6 oocytes after retrieval and ≥ 5 fertilized oocytes on Day 1 but failing to reach embryo transfer during two consecutive IVF cycles with embryo development arrest at the time of 2- to 4-cell cleavage stage were finally evaluated (n= 39). The inclusion criteria was female age of < 40 years and exclusion criteria was male factor necessitating surgical sperm retrieval. To generate controls among tubal factors, female age (± 1 year) and antral follicle (± 2) matched patients who had undergone IVF treatment in the same study period in whom embryos were incubated single step culture medium with human albumin solution (Sage 1-Step, Origio) were identified (n=80). Primary outcome was clinical pregnancy rate. **Results:** The mean female age, antral follicle count and anti-Müllerian hormone (AMH) level were comparable among the study group and controls. The mean numbers of oocytes cumulus complexes collected were 6.3 ± 3.0 and 7.0 ± 3.0 in GM-CSF group and controls, respectively (p= 0.292). The respective figure for mean number of fertilized oocytes (2-pronuclear) was 3.7 ± 2.0 and 3.9 ± 2.5 (p= 0.576). Mean number of embryos transferred were 1.3 ± 0.5 in both groups. Whereas embryo transfer on Day 5 was available in 67.6% of patients in study group, 59.2% achieved to reach blastocyst stage in controls (p= 0.560). Implantation (32.3% vs. 33.1%, p= 0.937) and clinical pregnancy rates per embryo transfer (33.3% vs. 32.5%, p= 0.770) were also statistically similar among patients in whom embryos were incubated in GM-CSF supplemented culture medium and controls. **Conclusion:** In patients with history of recurrent failed IVF attempts due to arrest in embryo development in spite of optimal number of oocytes retrieved and fertilization rate, supplementation of GM-CSF to culture medium might rectify pregnancy rates when compared with patients suffering from tubal infertility.

OP1-210

ULIPRISTAL ACETATE INHIBITS LEIOMYOMA CELL GROWTH VIA TGF- β SIGNALING PATHWAY

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Problem statement: Uterine leiomyomas (ULs) are the most common benign gynecological tumors. Due to poor understanding of their underlying pathobiology no effective pharmacological

treatment is currently available. Fibrosis and steroid hormones - especially progesterone (P4) are believed to be crucial in leiomyomas development. Nowadays, ulipristal acetate (UA), selective progesterone receptor modulator (SPRM) seems to be the most promising agent due to its strong antagonist activity to the nuclear progesterone receptor (PGR). Exact molecular mechanism of UA action in leiomyoma cells is not fully understood. Transforming growth factor- β (TGF β) as one of the most important factor of fibrosis may be involved in UA action in leiomyoma cells. The aim of our study was to analyze the effect of UA on TGF β signaling pathway in ULs. **Methods:** The evaluation was performed on tissue specimens obtained through myomectomy from UA-treated (n=30) and UA-untreated (n=50) patients with leiomyomas. The control group was a normal myometrium (n=50) obtained through hysterectomies performed for other reasons than leiomyomas. Immediately after surgery explants and primary cells (n=10) were established. Cultured cells were exposed to UA, P4, TGF β receptors inhibitor, SMAD3 inhibitor and combinations thereof. Cells viability was measured by MTT assay. Gene expression in cells and tissue were determined by qRT-PCR. Translocation of SMAD3 in leiomyoma cells was assessed by immunocytochemistry. The explants release of TGF β was analyzed by ELISA. **Results:** UA significantly inhibited leiomyoma cell growth and reversed the effect of P4. Leiomyoma cells expressed significantly higher level of TGF $\beta 1$, TGF $\beta 3$, TGF $\beta R2$ and SMAD3 compared with normal myometrium. UA treatment significantly downregulated TGF $\beta 1$, TGF $\beta 3$, TGF $\beta R2$, SMAD3 expression and TGF $\beta 1$ and TGF $\beta 3$ release in leiomyoma cells. SMAD3 inhibitor revealed strong inhibition of P4 action in ULs. Inhibition of TGF β receptors enhances the effect of UA in leiomyoma. Moreover, UA inhibited SMAD3 nuclear translocation in leiomyoma cells. **Conclusion:** Our results suggest that leiomyoma growth inhibition induced by UA may be mediated through TGF β signaling pathway. Moreover, SMAD3 may be a future target in ULs treatment.

OP1-301

PREGNANCY OUTCOMES IN RHEUMATIC DISEASES: A SINGLE CENTER EXPERIENCE

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Problem Statement. Pregnancy in rheumatic diseases is still often considered a problem due to the risk of poor outcomes. Recent studies had demonstrated that, when the disease is controlled, outcomes are the same as for the general pregnancies. Our aim is to review the pregnancy outcomes in women with rheumatic diseases in our Department. **Methods.** We retrospectively studied women with Rheumatoid Arthritis (RA), Systemic Erythematosus Lupus (SLE) and Spondyloarthritis (SPA) followed at Rheumatology Department. 296 of them agreed to give their data. Births outside our hospital were excluded because of the missing data. Were identified pregnancies and evaluated age at birth, disease activity at conception (Disease Activity Score - DAS for RA, Systemic Lupus Erythematosus Disease Activity Index- SLEDAI for SLE and Bath Ankylosing Spondylitis Disease Activity Index - BASDAI for SPA), pregnancy outcomes (number of live births, miscarriages, foetal deaths, premature births and pre-eclampsia), presence of antiphospholipid syndrome (APS) and Apgar index. **Results.** We identified 42 pregnancies in 33 women (12 with SLE, 15 with SPA and 6 with RA). Mean age at conception of 32.9y. Mean DAS28 was 2.27, mean SLEDAI was 3 and mean BASDAI 3,3 for RA, SLE and SPA, respectively. Twenty-seven pregnancies resulted in live births and 7 pregnancies resulted in pre-term babies. Occurred 6 miscarriages, one ectopic pregnancy and one



fetal death. All miscarriages occurred in SLE patients, four in the same patient (with MTHFR mutation) and the other 2 in patients with SLE and secondary APS. All babies had good Apgar (9-10), without congenital malformations. One pregnancy was complicated by pre-eclampsia (SLE). **Conclusion:** All pregnancy had excellent outcomes with exception for SLE patients. In the particular case of SLE, miscarriages and pre-term babies occurred only when the activity of the disease was uncontrolled or in the presence of a hypercoagulability state. A better management of SLE, including a closer monitoring of patients, their treatments and disease activity before conception and during pregnancy, is needed to improve outcomes in lupus pregnancies. Our center has now created a team of doctors (obstetricians and rheumatologists) that follow these patients in the same medical appointment.

OP1-302

SUCCESSFUL EMERGENCY CERCLAGE AT NINE WEEKS GESTATION IN WOMAN WITH HABITUAL ABORTIONS AND INTRAUTERINE ADHESIONS.

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OBJECTIVE: To report a rare case of emergency cervical transvaginal cerclage at nine weeks of gestation, presented with cervical dilatation and prolapsed membranes at 8 weeks of gestation. **Study Design: case report: CASE REPORT:** A 30-years-old woman, G7 P0 Ab6, was referred to our hospital with painless vaginal bleeding at eight weeks of gestation. She had a poor obstetric history of recurrent early miscarriages with repeated dilatation and curettage procedures at all them, and five operative hysteroscopies because of severe intrauterine adhesions. On physical examination the cervix was dilated to 2 cm with bulging membranes. Transvaginal ultrasound confirmed a singleton intrauterine pregnancy with crown rump length appropriate for gestational age (Figure 1). The uterine cavity was distorted with gestational sac observed in the isthmic part of the uterus. After consultation with the couple emergency cerclage at nine weeks of gestation was performed. Foley catheter was inflated up to 5 ml until membranes were pushed back from the cervix, and McDonald's technique was performed using Mersilene tape. **Results:** At 27 weeks she was admitted due to preterm premature rupture of membranes. After 2 weeks of conservative management, uncomplicated cesarean section was performed because of fetal growth restriction and severe oligohydramnios. A 950 g female infant was delivered, supported by eight days of noninvasive ventilation, and was discharged after 48 days. She is now six months old and doing well. **Conclusions:** In women with recurrent surgical cervical dilation who present with first trimester cervical insufficiency, early emergency cerclage may be of beneficial. We believe in individual management approach according to its specific circumstances before making decisions, even if it's not the acceptable timing and the known approach. To our knowledge this is the first case reported in the literature of first trimester emergency cerclage for cervical dilation.



OP1-303

PREGNANCY OUTCOMES AFTER LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE – IS IT REALLY THAT RISKY?

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Problem statement: Large loop excision of the transformation zone (LLETZ) for high-grade lesions of the cervix is carried out in many women of reproductive age who still want to become pregnant. However, a pregnancy following such a procedure has been considered as being high-risk, given the apparently increased rates of preterm delivery, short cervix and low birth weight infants. We studied the outcomes of 118 pregnancies in women who had previously undergone LLETZ to assess the prevalence of these complications. **Methods:** We conducted a retrospective study in all women who underwent LLETZ in our department between January 2005 and June 2018, to assess outcomes and complications of pregnancies occurring after the procedure. We accessed their paper and electronic medical records on local and national platforms and interviewed them by phone to complete missing data. **Results:** Out of 691 women who underwent LLETZ, 91 (13%) became pregnant afterwards; of these, 24 had more than one pregnancy. There was a total of 118 pregnancies, including 24 first trimester miscarriages, 1 second trimester miscarriage (due to malaria complications), 2 ectopic pregnancies, 6 voluntary terminations, 8 preterm deliveries and 68 term pregnancies; the remaining nine are still ongoing. Regarding the 76 completed gestations (term and preterm), the average maternal age at delivery was 33 years; the average interval between LLETZ and delivery was 34 months for preterm versus 39 months for term deliveries (nonsignificant: $p=0,58$). Four women had undergone repeat LLETZ before getting pregnant, all of whom had term deliveries. The average gestational age at delivery was 38,3 weeks (median 39 weeks, standard deviation 2,3 weeks). There were five pregnancies complicated by threatened preterm labour: two had term deliveries, whereas the other three ended at 36 weeks. The remaining 5 preterm deliveries were unrelated to short cervix. There were 71% of vaginal deliveries and 29% of cesarean sections. The average newborn weight was 2993 grams (± 573 grams). None of the women required cervical cerclage. **Conclusion:** In our sample, LLETZ for high-grade lesions of the cervix did not seem to increase adverse pregnancy outcomes, including threatened or actual preterm labour, short cervix or low birth weight.

OP1-304

MATERNAL DIETARY PATTERNS DURING PREGNANCY AND OFFSPRING SIZE AT BIRTH: A SYSTEMATIC REVIEW OF THE EVIDENCE

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Problem statement: The purpose of this review was to examine and synthesise the evidence base relating to the potential impact of maternal dietary patterns during pregnancy on offspring size at birth. **Methods:** MEDLINE, Cochrane library, EMBASE and Maternity and Infant Care were searched up to August 2018 for studies reporting associations between dietary patterns in pregnancy and offspring size at birth in low risk pregnant populations. Due to heterogeneity of studies a meta-analysis was not performed. Aspects of study quality, including appropriateness

of study design, method of dietary assessment, dietary data analysis, outcome measures and statistical techniques used were assessed. **Results:** The search identified 5,060 references of which 359 were retrieved for further evaluation with 33 meeting the inclusion criteria. Thirty studies were of a prospective cohort design, one of a case-control and two of a cross-sectional design. All varied in terms of sample size (from N=41 to N=66,597), exposure and outcome measures, dietary pattern analysis and statistical analysis. All but one study assessed dietary patterns that somewhat conformed to current guidelines on healthy eating (e.g. Mediterranean diet, Nordic Diet, Healthy Eating Index (HEI), The Dietary Approaches to Stop Hypertension (DASH) diet, or a posteriori derived patterns containing healthy foods). The evidence was most convincing for birth weight (expressed in grams as well as FGR and SGA), with the HEI showing the strongest association, where mothers with a dietary pattern that scored highly on the HEI had offspring with the biggest increase in birth weight (126 g) and the greatest reduction in risk of FGR (76 % reduced odds). Evidence for more unhealthy dietary patterns, characterised by high intakes of processed food, refined grains and sugary foods and drinks was less uniform. **Conclusion:** Findings were somewhat in agreement with the hypothesis that optimal perinatal nutrition leads to favourable size at birth. This review helps to identify the methodological challenges in this area of nutritional epidemiology and will help researchers make informed decisions in regard to future analyses. It is clear that a more uniform approach to dietary pattern analysis is needed in order to facilitate in between study comparisons.

OP1-305

EFFICACY AND SAFETY OF ISOXSUPRINE HYDROCHLORIDE AS UTERINE RELAXANT IN PRETERM LABOR – A PROSPECTIVE, OPEN-LABEL, NON-COMPARATIVE STUDY [FIRST ANALYSIS RESULTS]

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Problem Statement: Preterm labor (PTL) is the leading cause of perinatal morbidity and mortality, with an incidence of 23.3% in India. Diagnosis has always been the challenge and tocolytics remains the mainstay in the treatment. Recent American College of Obstetricians and Gynaecologists guidelines recommend beta-adrenergic agonists therapy as the first line tocolytic agent. Hence this study was conducted to assess the short and long term safety and efficacy of isoxsuprine hydrochloride as a tocolytic agent in the management of PTL. **Methods:** In this first analysis report, data from 40 patients (from planned enrollment of 50) presented in PTL (active/threatened) between 24-37 weeks of gestation are included. All participants were given loading dose of isoxsuprine-40 mg infusion (i.v) (500 ml of 5% dextrose at a concentration of 0.8mg/ml). Drop rate was set at 8 drops/minute (0.04 mg/minute), which was increased by 8 drops every 15-minutes until uterine quiescence. After 15 minutes of infusion stoppage, isoxsuprine-10 mg/4 hourly (i.m injection) was given up to first 24-hours of hospitalization. For next 24 hours, isoxsuprine-40mg retard oral capsule was given as a maintenance therapy and the same oral dose was continued till the time of delivery. Efficacy (successful tocolysis in 48-hours, total latency period, birth weight, Apgar score) and tolerability was assessed based on the patient/physicians' assessment of wellbeing after medication. Data were analyzed using SPSS software. **Results:** Mean (\pm SD) age of the participants was 24.4 \pm 3.3 years. About 62.5% patients were multigravida. Mean (\pm SD) gestation age at baseline was 31.5 \pm 2.7 weeks and at delivery was 39.6 \pm 2.2 weeks. Successful tocolysis in 48-hours was achieved in all patients (100%). Total latency period was 57.5 \pm 18.5 days. Mean (\pm SD) fetal birth weight was 2.7 \pm 0.4Kg. Apgar score at 1 min was found to be 7.3 \pm 0.6 and at 5 min was 9.2 \pm 0.4. Most commonly reported adverse events were maternal

tachycardia (7.5%) and nausea (5.0%) (during first 24 hours of iv/im therapy). However, no adverse effects were reported during maintenance treatment with oral isoxsuprine retard capsules. **Conclusion:** Isoxsuprine was found to be an effective and well-tolerated tocolytic agent in arresting PTL, in turn resulting in improvement in maternal and perinatal outcomes.

OP1-306

PRELIMINARY RESULTS FROM THE NATIONWIDE AUSTRIAN REGISTER FOR REPRODUCTION AND RHEUMATIC DISEASE (RHE PRO REGISTER)

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Problem statement: Data is limited regarding pregnancies and family planning with inflammatory rheumatic diseases. In May 2017, -in the hope to collect more experience and data in this topic the nationwide Austrian Register for Reproduction and Rheumatic disease (RhePro Register) was established at the Medical University of Vienna. **Methods:** The RhePro Register is a prospective nationwide, web-based longitudinal observational cohort study. Pregnant patients with confirmed diagnosis of inflammatory rheumatic disease are eligible to be enrolled until the 20th week of pregnancy or patients who wish to conceive. Clinical and laboratory course of rheumatic disease, the course of pregnancy, maternal and fetal complications during and after pregnancy and information of pharmaceutical treatment throughout the pregnancy and 3 years postpartal will be documented and collected. The collected data is pseudoanonymized and data handling is conform with the data protection policy. **Results:** The RhePro Register started on 15th of May 2017. Up to now there are 6 recruiting centers. Until the end of January 2018, 89 patients were recruited. 36 pregnant women delivered their children, 17 women are currently pregnant and 36 women are in praeconceptional care. Of these patients 31 suffered from systemic lupus erythematosus, 11 from Sjögrens syndrome, 7 had other connective tissue diseases, 22 rheumatoid arthritis, 10 spondyloarthritis, 2 juvenile idiopathic arthritis, 2 psoriatic arthritis, and 3 systemic vasculitis. Average birthweight of the newborn was 2895gr, average gestations week at delivery was 38 weeks. 9/36 (25%) of the newborn were either small for gestational age (n=7 SGA) or had an intrauterine growth restriction (n=2 IUGR) and 75% of the newborn were appropriate for gestational age (AGA) at delivery. Pregnancy complications included 1 HELLP syndrome, 6 patients experienced preterm delivery before gestational week 37, one patient had a postpartal deep venous thrombosis, 6 newborn were admitted to the neonatal intensive care unit postpartal, one child had a complex heart malformation. **Conclusions:** The Austrian RhePro Register is launched. We hope to contribute to the present knowledge of patients with inflammatory rheumatic disease and pregnancy or present family planning. The authors have no conflict of interest.



OP1-307

MATERNAL SERUM MATRIX METALLOPROTEINASE 14 (MMP14) IN PREECLAMPSIA AND NORMAL PREGNANCY WOMEN: ALTERNATIVE BIOMARKER OF PREECLAMPSIA

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Problem statement: Matrix Metalloproteinases 14 presumably play a major role in preeclampsia incident through endoglin cleavage process and have reported that MMP14 expressions increased in preeclamptic placenta. Up until today, no studies have been conducted in investigating whether MMP14 can be used as biomarker of preeclampsia. The aim of this study was to analyze whether maternal serum matrix metalloproteinases 14 levels differ in preeclampsia and uncomplicated pregnancies. **Methods:** This cross sectional study was carried out in 35 subjects with preeclampsia and 35 subjects of normotensive pregnant women range 24 up until 40 weeks of gestation. The study was conducted in Margono Hospital Purwokerto, Indonesia. Level of MMP 14 was measured in maternal serum using an enzyme-linked immunosorbent assay (ELISA). The mean difference was statically analyzed by independent samples T-test and ROC curve to determine sensitivity and specificity of MMP 14. **Results:** Women age, parity, gestational age and body mass index showed a non significant difference between both groups. In this study level MMP 14 in serum was higher in pregnant women with preeclampsia compared to the normotensive (284.43 vs 58.44 pg/ml ; p0.00). Moreover, the area under the curve (AUC) of serum MMP 14 was 0.95 [95% confidence interval (CI): 0.902–0.999, P0.001]. The optimal cut-off value of serum MMP at 94,69 pg/ml showed a high diagnostic value in preeclampsia with a sensitivity of 97.1% and a specificity of 82.9%. **Conclusion:** The level MMP 14 in serum was higher in pregnant women with preeclampsia. The important finding is the MMP 14 probably become a marker in preeclampsia. **Keywords:** preeclampsia, normal pregnancy, Matrix Metalloproteinase 14, MMP14. The authors have no conflicts of interest to disclose relative to the contents of this presentation

OP1-308

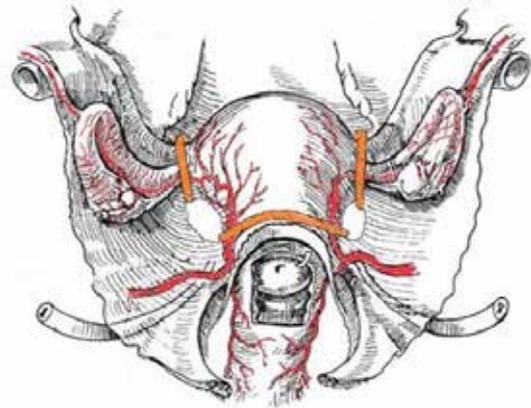
ALTERNATIVE APPROACHES TO SURGICAL HEMOSTASIS IN PATIENTS WITH MORBIDLY ADHERENT PLACENTA UNDERGOING FERTILITY-SPARING SYRGERY

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Problem statement: Since 1960 the incidence of morbidly adherent placenta (MAP) increased from 1 in 30,000 pregnancies to 1 in 533 cases, which correlates with an increase in the frequency of abdominal delivery. MAP increased by 7% in the structure of maternal mortality. This fact is explained of a higher degree of the uterus wall vascularization with the large vessels in the invasive area. There are two main approaches that are managed these patients: one-stage or delayed hysterectomy and a more progressive tactic, implying an organ-preserving treatment. **Methods:** The study included 54 patients with MAP. All patients underwent cesarean section with application of surgical hemostasis techniques. In Group 1 (n=15), ligation of IIA was performed, in Group 2 (n=18) – temporary occlusion of CIA, and in Group 3 (n=21) – combined compression hemostasis was applied (Figure 1). The latter technique included placement of bilateral tourniquets on the upper uterine pedicles and on the cervicoisthmic segment, and controlled Zhukovsky balloon tamponade of the uterus, with subsequent resection of the uterine wall with abnormal

placental invasion, evacuation of placenta from the uterine cavity and closure of the uterine wall defect with a double suture. The studied outcomes were: total blood loss, duration of surgery, the hemoglobin level alteration, hysterectomy rate, and length of postoperative hospital stay. **Results:** Total blood loss in Group 1 was 2440±1215 ml, in Group 2 – 2186±1353 ml, and in Group 3 – 1295±520.3 ml (P=0.0045). In Group 3, the lowest number of cases with blood loss 2000 ml was observed [8 (53.3%) versus 9 (50.0%) and 2 (9.5%), respectively; P=0.0411]. The duration of surgery, the hemoglobin level alteration, hysterectomy rate, and length of hospital stay after delivery did not differ significantly between the groups. **Conclusion:** The most effective way to reduce blood flow in performing an organ-preserving surgical delivery in a patient with MAP is a complex compression hemostasis. The received data confirmed the fundamental works describing the actively functioning anastomotic networks in projections of the connection of the terminal branches of the uterine and ovarian arteries, as well as numerous communications in the isthmus-vaginal area.



OP1-309

ACTIVE VERSUS EXPECTANT MANAGEMENT IN WOMEN WITH SEVERE PREECLAMPSIA

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Problem statement. Comparison of obstetric and neonatal outcomes in women with early severe preeclampsia, depending on the management of pregnancy. **Methods.** The health of 45 women with early severe preeclampsia and their newborns was analyzed. Women were divided into 2 groups. 1st group contained 25 pregnant women with expectant management and 2nd group - 20 women - with active. 1 group was divided into 2 subgroups depending on the CPAP therapy – use. 1A subgroup contained CPAP therapy in addition to standard treatment (n = 12) and 1B subgroup was managed without CPAP (1B) (n = 13). **Results.** In group 1, the main indication for delivery was worsening of the fetus - negative or zero blood flow in the umbilical artery or in the ductus venosus (7 (58%) in the 1A group, 3 (23%) - 1B) and the increase in the severity of the PE, despite intensive therapy (4 (33%) in the 1A group and 9 (69%) in the 1B group). Indication for delivery in the group 2 was from mother's side. The analysis of the newborns outcomes in patients with severe PE revealed that their anthropometric parameters at birth were lower in group 1A, caused by more earlier term of delivery. However, despite the earlier time of delivery in the 1A group, the need for invasive methods of respiratory support in newborns was lower (8.3%), while in Group 1B, standard ventilation was used in 30.7% of cases, and in group 2 - in 40%, and the need for surfactant administration was 66, 6%

and 84% in 1A and 1B groups respectively, and 75% in the group 2. The stay in the NICU and postnatal mortality did not differ. Hemorrhagic syndrome in the 1A group was 41.6%, in the 1B group 30.7%, against 70% in patients from the 2 group. Necrotizing enterocolitis was more common in newborns of the 2nd group (35% of cases). **Conclusion.** It is necessary to further monitor and analyze the outcomes of the mother and newborn in the expectant management of preeclampsia in order to improve the prognosis and the possibility of pregnancy prolongation.

OP1-310

LOW MATERNAL CONCENTRATIONS OF HUMAN CHORIONIC GONADOTROPIN (hCG) IN EARLY PREGNANCY; AN INDICATOR OF INCREASED RISK OF ADVERSE PREGNANCY OUTCOME?

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Problem statement: Human chorionic gonadotropin (hCG) is synthesized in trophoblastic cells in the placenta. Shortly after implantation of the embryo into the endometrium, hCG may be detected in maternal blood. The maternal hCG concentration normally increases rapidly after implantation and until pregnancy week 10. Low hCG concentration in very early pregnancy is likely to indicate delayed embryo implantation or impaired proliferation of trophoblastic cells. We studied the associations of maternal hCG concentration in early pregnancy with the risk of preeclampsia and with cerebral palsy (CP) in the offspring. **Methods:** To study the risk of preeclampsia, we performed two follow-up studies, and we obtained information about development of preeclampsia by individual linkage to the Medical Birth Registry of Norway. Study i) included 2405 pregnancies after in vitro fertilization (IVF) at Oslo University Hospital, and hCG was quantified at day 12 after embryo transfer. Study ii) was a nested case control among 29948 pregnancies in the Toxoplasmosis Study Registry (279 cases with preeclampsia and 356 controls), and hCG was quantified at week eight of pregnancy (mean). To study the association of maternal hCG concentration with CP in the offspring, the Toxoplasmosis Study Registry was linked to the Norwegian Registry of Children with CP (nested case control study, 78 cases with CP and 199 controls). **Results:** We found that low hCG concentration (lowest quartile of the distribution) in early pregnancy doubled the risk of preeclampsia as compared to hCG concentration in the highest quartile. Low hCG concentration increased the risk for severe preeclampsia in particular (almost fourfold increase). Additionally, low maternal hCG concentration in early pregnancy seemed to increase the risk for CP in the offspring. **Conclusion:** We found that low maternal hCG concentration in early pregnancy was associated with increased risk of preeclampsia in the mother and of CP in the offspring. Low hCG concentrations in early pregnancy is likely to indicate delayed embryo implantation and/or impaired trophoblast proliferation. Impaired trophoblast proliferation could cause impaired placental function and suboptimal oxygen supply to the fetoplacental unit, and possibly explain the mechanisms behind the observed associations.

OP1-401

DETECTION OF HUMAN PAPILLOMA VIRUS AND EPSTEIN BARR VIRUS IN SQUAMOUS CELL CARCINOMA OF THE CERVIX

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Problem statement: Worldwide, cervical cancer is second most common cancer and the fifth deadliest cancer in women. Other risk factors include smoking, human immunodeficiency virus. **The Epstein-Barr virus (EBV)**, is a virus of the herpes family. When infection with EBV occurs during adolescence, it causes infectious mononucleosis 35 to 50 percent of the time. EBV infects B cells of the immune system and epithelial cells. This study aimed to detect HPV and EBV in squamous cell carcinoma of the cervix. **Methods:** This study was prospective case control study. Samples were collected from different histopathology laboratories. Collected samples were transferred to histopathology lab where they were processed and examined. Questionnaire sheets were used to record all patients and samples data. Three sections were cut from each tissue block using Leika microtome, each section measure four micrometers. Results analyzed using (SPSS) version 17.0. **Results:** 26 biopsies of Squamous cell carcinoma (SCC) were analyzed (47.4%) had low and high-risk HPV strains in (47.4 %) and (52.6%) free HPV and EBV. In the same biopsies, the EBV antigen was detected by using immunohistochemistry and specific tumor marker LMP-1 antigen was detected in (52.6 %) in positive case with SCC, but EBV was (28.6%) in control sample. Also HPV antigen by using immunohistochemistry method specific tumor marker Ab-3 which expressed in (84.2%) positive case of SCC and 15.8 % free from HPV. **Conclusion:** This is first study preliminary presented results of EBV and HR-HPV co-infection in Africa compared to North American, Thailand and Japanese SCC cases which were recently reported. In our hands we showed that most SCC patients were HPV infected followed HPV-EBV co-infected. A possible joint effect of the two viruses on cervix tumor development should be considered. Such hypothesis is strengthened by EBV oncogene expression. It is clear that the presence of EBV and its relationship with HPV in cervical oncogenesis need to be further investigated. This study recommended that more study should be done with more sample size using advance specific and sensitive methods such as real-time polymerase chain reaction to detect suspected risk factors associated with cervical cancer.

OP1-402

HUMAN PAPILLOMAVIRUS DETECTION IN SELF-SAMPLING VERSUS CLINICIAN-COLLECTED SAMPLES OF VAGINAL DISCHARGE: EFFICIENCY, ACCEPTABILITY AND PREDICTIVE VALUE

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Problem statement: Human papillomavirus (HPV) is a group of viruses that are extremely common worldwide. Cervical cancer is by far the most common HPV-related disease (WHO, February 2018). The aim of this study was to evaluate the acceptability, efficiency and predictive value of high-risk HPV (HR-HPV) in self-collected using the Qvintip device versus clinician-collected samples in vaginal discharge. **Methods:** A cross-sectional study involving 200 women (mean age 32.7±6.9, range 18–45 years) attended to an outpatient clinic for annual medical examination. Vaginal discharge was collected using an Qvintip device and vaginal smear from the cervical canal was taken by a physician for



a further HR-HPV PCR test. The predictive value of these techniques was evaluated according to generally accepted formulas. An interviews using to assess acceptability. **Results:** 42% of all patients were HR-HPV positive. The efficiency of the survey using the self-collected Qvintip device was higher than the clinician-taken samples: 38% vs 27.5% (OR=1.6; 95% CI 1.18-2.45). HPV16 was the most frequently encountered HPV type (17.7%). 51.2% of HPV-positive women were infected with several types of HR-HPV. Self-sampling using the Qvintip device was a well-accepted method. Compared to physician-sampling, women reported a preference for self-sampling, as it was more comfortable (75% vs 22.2%, $p=0.001$) and caused less pain (70.3% vs 22.2%, $p=0.001$) and less embarrassment (25.8% vs 1.4%, $p=0.001$). 84.7% of women preferred clinician-collected vaginal samples because they thought it was more properly taken. Most preferred to take the self-sample at home in the future (96%) because it was simple and did not require a doctor's appointment. LSIL and HSIL were diagnosed only in HPV-positive women (15.5% and 2.4% respectively, $p=0.000$). When the material was taken by a woman using an Ovintip device, the sensitivity and specificity of HR-HPV diagnosis were 72.2 and 90.8%, respectively. **Conclusion:** Our study results demonstrated a high rate of HR-HPV infection (42%) among reproductive age women. Vaginal self-sampling using the Qvintip device was easy and comfortable, and shown high diagnostic efficiency and prognostic value, and complacency of patients. Self-collection of the sample could be used as an alternative for HR-HPV detection.

OP1-403

VAGINAL INVOLVEMENT AS AN INDEPENDENT PREDICTOR OF OUTCOME IN FIGO STAGE IIB AND IIB CARCINOMA CERVIX - A SINGLE INSTITUTIONAL RETROSPECTIVE STUDY

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Problem statement: Vaginal involvement (VI) is not adequately represented in the current FIGO staging of carcinoma cervix (CACX) stages IIB and IIIB which constitute the majority of patients in our clinical practice. With the advent of MRI, better delineation and consequently dose volume prescription and evaluation of the vagina is evolving. The objective is to assess whether disease outcomes depend on the presence of VI at presentation, specifically in FIGO Stage IIB & IIIB cervical carcinoma patients receiving standard treatment. **Methods:** In this single institutional retrospective study, records of 339 consecutive patients registered between January 2014 and December, 2015 with CACX FIGO Stage IIB or IIIB irrespective of VI, who completed the course of standard concurrent chemo-radiation followed by HDR brachytherapy were analysed. Response was assessed using Response Evaluation Criteria In Solid Tumours (RECIST v1.1). Median Progression Free Survival (mPFS) stratified by VI was analysed using Kaplan Meier Survival Plot. **Results:** At diagnosis, out of 339 patients 170 were stage IIB and 169 were stage IIIB CACX. VI was evident in 51.2% IIB and 74.6% IIIB patients. After standard treatment, at a median follow up of 42 months, mPFS for FIGO stage IIB were 35 months (without VI) vs 28 months (with VI) and for FIGO stage IIIB mPFS were 32 months (without VI) vs 26 (with upper VI), 18 (with middle VI) & 15 (with lower VI) months with significant log rank $p=0.001$. Irrespective of FIGO stage mPFS were 33 months (without VI) vs 26 (with upper VI), 25 (with middle VI) & 16 (with lower VI) months with an again significant log rank $p=0.001$. **Conclusion:** VI appears to be an independent poor predictor of outcome for locoregional control in FIGO stages IIB and IIIB CACX. Unfortunately the current FIGO staging does not incorporate this. We therefore propose to suggest modification of the existing FIGO stage IIB and IIIB to include CACX patients with parametrial involvement only without vaginal involvement and to

incorporate two new stages IIC and IIIC respectively for patients who have involvement of both vagina and parametria at presentation.

OP1-404

FIRST TRIMESTER POST-ABORTAL PLACENTA INCRETA: A CASE REPORT

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Introduction: Obstetrical hemorrhage is one the leading causes of maternal morbidity and mortality in our country. It accounts for 298 out of 1,719 women (17.3 %). Obstetrical complications such as hemorrhage may ensue once the placenta adheres into the myometrium and was not noted during placental delivery. **Case Report:** This is a case of a 30 year old, Gravida 3 Para 1 (1021), who had persistent vaginal bleeding post curettage due to missed abortion at 11 weeks age of gestation. She came in at our institution with an elevated beta human chorionic gonadotrophic hormone and transvaginal ultrasound with an impression of retained products of conception versus invasive mole. She had stable vital signs and with pink conjunctiva. Abdomen was flabby and soft. Speculum examination revealed a clean looking cervix with scanty brownish vaginal discharge. Internal exam revealed a firm and closed cervix, slightly enlarged uterus, and with no adnexal mass or tenderness. **Case Discussion:** Differential diagnosis included retained secundines, gestational trophoblastic neoplasia, uterine arteriovenous malformation, and placental accrete syndrome. This could be differentiated by beta human chorionic gonadotrophic hormone and transvaginal ultrasound. What made the case interesting is the dilemma in the diagnosis. In a case of persistent vaginal bleeding after curettage and with a history of cesarean delivery, one will initially think of placenta accrete syndrome. But then, initial diagnostic tests on admission pointed out to uterine arteriovenous malformation. Due to the dilemma of the service team in clinching the diagnosis for a single disease entity, pelvic magnetic resonance imaging with contrast was done revealing a possible placenta accreta, but cannot totally rule out vascular tumor. Since patient was initially desirous of future pregnancy, medical management was started and was scheduled for CT angiography. However, due to persistent vaginal bleeding, she underwent Total Abdominal Hysterectomy. Histopathology result revealed a placenta increta. **Conclusion:** In the advent of technology, a wide array of diagnostic modalities can be used to make an appropriate diagnosis. Clinical correlation and a high index of suspicion must be at all times considered above all.

OP1-405

COMPREHENSIVE MULTIDISCIPLINARY MANAGEMENT OF MALIGNANT OVARIAN GERM CELL TUMORS AND FETO-MATERNAL OUTCOME: SERIAL CASE REPORT

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Problem Statement: Malignant Ovarian Germ Cell Tumors (MOGCT) most commonly occur in young women in the reproductive age group which usually unilateral and usually diagnosed at Stadium I. The incidence of MOGCTs is less than 5% of all ovarian cancers arising from germ cells of the ovary. The most common MOGCT is the dysgerminoma, following by teratoma and yolk sac tumor (1-2% of all malignant ovarian tumors). Timely antenatal diagnosis and treatment of the tumor to enhance maternal and perinatal outcomes are the main challenges confronting the obstetrician and the gyne-oncologist. **Methods:** This study was a case report, which in it we had already done in the clinical setting as comprehensive multidisciplinary approach with regard to diagnosis, primary surgery, chemotherapy, delivery, complete surgical staging, and neonatal care. **Results:** In this article, we present three case reports of MOGCTs in pregnancy and do chemotherapy intervention in third semester and getting some various complication. The first case (immature teratoma) was complicated by maternal psychological symptoms consistent with stress which is ovarian atrophy and histopathological examination confirmed the diagnosis of premature ovarian failure (POF). The second case (dysgerminoma) preterm labor occurred as an obstetric complication but the baby was born in good condition without IUGR. The third case (yolk sac tumor) treated with docetaxel (brexel)-carboplatin chemotherapy administration there was no maternal or fetal complication. All the babies were of normal weight. Laboratory findings at the first week after birth did not find any evidence of transient myelo-suppression. At the end of the pregnancy and delivery, a complete surgical staging and cytoreduction was performed and no metastases were found. **Conclusion:** Optimal management strategies center on a multi disciplinary comprehensive team approach is critical resulting in better outcomes for mother and the baby by avoiding complications. **Keywords:** Ovarian malignant germ cell tumors, pregnancy, chemotherapy, surgical staging

OP1-406

MUSCLE-SPARING SKIN-REDUCING BREAST RECONSTRUCTION WITH PRE-PECTORAL IMPLANTS IN BREAST CANCER PATIENTS: LONG TERM ASSESSMENT OF PATIENTS' SATISFACTION AND QUALITY OF LIFE

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Problem Statement: Worldwide, breast cancer is the most frequent malignancy diagnosed in women and the second most common type of cancer after lung cancer, accounting 23% of all cancer deaths. With the development of genetic testing, progresses in reconstructive and imaging techniques and growing relevance of breast reconstruction in media, the number of women undergoing mastectomy for prophylaxis has enhanced, also contributing to the rise in demand for immediate breast reconstruction after mastectomy. Breast reconstruction can improve patients' quality of life (QoL) and alleviate the psychological distress related to the disease and the radical operation. The aim of this study was to investigate pre- and post-operative assessment of quality of life and aesthetic satisfaction in patients with breast cancer undergoing muscle-sparing skin-reducing breast reconstruction (MS-MR) with pre-pectoral implants. **Methods:** Patients presenting to the Unit of Plastic Surgery of the Universities of Pisa and Sapienza of Rome suitable for MS-SR breast reconstruction satisfying specific oncological and reconstructive criteria were enrolled in the study. Specific questionnaires (EORTC QLQ-C30, QLQ-BR23) were administered preoperatively, 1, 6 and 12 months after surgery to evaluate patients' QoL. **Results:** A total of 63 women with breast cancer

underwent MS-SR. In 15 patients BR was bilateral, so a whole of 78 breasts were reconstructed with this technique. One month after surgery, both EORTC QLQ-C30 and QLQ-BR23 average scores demonstrated a slight pickup since preoperative values, but results on QoL improvement were significantly evident 12 months after BR (p0.0001). Physical and aesthetical satisfaction, assessed by the BREAST-Q test, showed significant scores upturn 12 months postoperatively respect to the immediate postoperative assessment (p0.0001). **Conclusion:** EORTC QLQ-C30 and QLQ-BR23 scales discriminated between pre-treatment and after treatment patients showing an improvement in general QoL and aesthetic satisfaction in women with breast cancer undergoing MS-SR breast reconstruction. Even further studies are needed to confirm those results, this new technique showed promising oncologic but also aesthetic outcomes, sparing the pectoralis major muscle thus improving significantly women QoL and well-being.

OP1-407

CIN 2-3 IN PREGNANCY -THE SAFETY OF LLETZ IN THE FIRST 15 WEEKS AND THE RISK OF CERVICAL CANCER.

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Problem Statement: Cervical Intraepithelial Neoplasia (CIN) grade 2-3 diagnosis in non-pregnant women lead to prompt treatment by Large Loop Excision of Transformation Zone (LLETZ).Pregnancy is considered a contraindication to LLETZ due to the conception that CIN 2-3 during pregnancy does not progress to invasive cancer, spontaneous remission is common and LLETZ during pregnancy carry a significant risk of severe complications as severe bleeding , abortions and premature delivery. We are describing our experience of patients with CIN 2-3 during pregnancy that underwent LLETZ during the first 15 weeks of pregnancy or were observed only. **Methods:** Data about 140 patients diagnosed during pregnancy between 2006-2018 with CIN 2 or CIN 2-3 on cervical biopsy was collected from a few medical centers in Israel. 27 women with CIN 2 and 63 patients with CIN 2-3 were conservatively followed up. 50 patients underwent LLETZ during the first 15 gestational weeks. We compared the outcome between the two groups. **Results:** In 7(6.2%) patients with CIN 2-3 during pregnancy, the final diagnosis was invasive cancer. The postpartum results in 63 women who were conservatively observed were: 4(6.4%) had cervical cancer ,43(68.2%) had CIN 2-3, 16(25.4%) had CIN 1 or normal histology .The diagnosis of the 50 patients who have undergone LLETZ was invasive cancer in 3 patients (6%) ,CIN 2-3 or Adenocarcinoma In Situ (AIS) in 44(89%) women [p0.01],and 3 women (6%) had CIN 1 or normal histology [p0.01].None of them suffered severe bleeding. 43 women continued their pregnancy, 39(90.7%) had term deliveries, two (4.6%) gave birth at 34 and 36 weeks and two (6%) had missed abortions. **Conclusions:** In 6.2% of women diagnosed with CIN 2-3 during pregnancy the final diagnosis was invasive cancer. The LLETZ operation during the first 15 weeks of pregnancy is safe. It is time to reconsider the recommendations about LLETZ treatment of CIN 2-3 lesions in early gestation.



OP1-408

HIGH CORRELATION BETWEEN CLEARANCE OF HR-HPV TYPES AFTER LLETZ IN EARLY STAGE CERVICAL CANCER AND ABSENCE OF RESIDUAL CANCER IN THE FINAL PATHOLOGICAL SPECIMEN

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Problem Statement: The standard treatment for early stage cervical cancer is radical hysterectomy(RH) and pelvic and paraaortic lymphadenectomy. Studies has shown that as much as 60% of patients wo underwent RT for stage 1 A2-1 B1 cervical cancer have no residual cancer in the final pathology specimen. We examined whether in women with cervical cancer stage 1 A 1 -1 B 1, positive for High Risk Human Papiloma Virus (HR-HPV) types ,clearance of HR-HPV has a high correlation with absence of cervical cancer in the final pathological specimen. **Methods:** Data was collected about 53 patients diagnosed with invasive cervical cancer stage 1A 1-1B 1 and positive for HR-HPV who underwent LLETZ operation. Shortly after the LLETZ a repeat HR-HPV test was performed from the cervix. The patients were treated according to FIGO guidelines and were scheduled for operation or chemo-radiation therapy. HR-HPV status was not considered before the decision about the treatment proposed. We compared characteristics of patients with negative or positive HR-HPV and investigated the association of post LLETZ HR-HPV status with residual cancer in the final pathology. **Results:** Of 53 patients ,22 were HR-HPV negative after LLETZ: On the final pathology specimen 17 (77.3%) had normal histology ,3(13.6%) had Cervical Intraepithelial Neoplasia(CIN) 3 and only 2 (9.1%) had residual cancer. In those patients the operations performed was: 6 simple hysterectomy ,9 RH ,2 radical trachelectomy ,3 repeat LLETZ and two women refused further operation and were followed up. Of the 31 women who were HR-HPV positive after LLETZ 8 (25.8%) were sent to chemo-radiation, The other patients were operated and the final histological results were invasive cancer in 13(41.9%) women ,CIN 3 in 6(19.4%) women and normal histology in 4 (12.9%) women. **Conclusions:** In 90.9% of women with negative HR-HPV after LLETZ there was no residual invasive cancer in the final specimen. Larger studies are needed to prove if negative HR-HPV after LLETZ might serve as a new parameter for risk assessment and for less aggressive surgery specially in women wishing to preserve their fertility.

OP1-409

RISK FACTORS AND THE APPEARANCE OF BREAST CANCER

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The aim: To investigate the occurrence of breast cancer using ultrasonic examination of the breast and to compare the possible risk factors, in the gynaecology clinic in Zadar, Croatia. **Method of work:** During the period from November 1, 2017 to August 31, 2018 the ultrasound breast examination and breast cancer risk factor survey included 446 women, 57 were under 30 years of age, 142 under 40, 110 under 50, 88 under 60, 49 over 60 years of age. The ultrasound breast examination was classified according to BI-RADS findings and age groups and the survey was conducted using a questionnaire on possible factors of breast cancer risk: sex, age, relatives, BReast CAncer genes 1,2, first menstruation, menopause, Oral Hormone Contraception, Hormone Replacement

Therapy, first pregnancy, breastfeeding, X-ray, weight in menopause, cigarettes. We analysed the breast of non-negligible women of different ages and parity. **Results:** In the tested period the ultrasound probe included 7.15% of women (446 of 6230 registered women). The BI-RADS1-2 was 98.65% (440/446), BI-RADS3 1.12% (5/446) and BI-RADS4 0.22% (1/446). According to age, BI-RADS1-2 was the highest in the age group 31-40, 31.61% (141/446). BI-RADS3 in the age group 51-60, 0.89% (4/446), while BI-RADS4 in the age group 41-50, 0.22% (1/446). It was proved by the puncture of 1 breast cancer, from BI-RADS4 findings 0.22% (1/446). The most frequent elevated risk was a period of breastfeeding (≤12 months) 33%, cigarettes (≥10 years) 19%, X-rays (≥2 computed tomography) 18%, first menstruation (≤11 years) 13.1%, menopause (≥55 years) 6.5%, positive history 4.9%, the other 5.5%. **Conclusion:** According to the ultrasound examination, the riskiest group was BI-RADS3, age group 51-60. The most common risk for breast cancer was breastfeeding for less than 12 months. We did not realize that the accumulation of risk factors increases the occurrence of breast cancer in our patients. **Keywords:** breast cancer, risk factors. BI-RADS - breast imaging reporting and data system

OP1-410

RECURRENCE RATES AFTER PELVIC GYNAECOLOGIC NEOPLASMS

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Problem statement: The authors wanted to know the level of trust of oncologic surgical procedures performed for gynecologic pelvic cancers .We made a study highlighting the loco-regional and lymph node recurrence, after the radical interventions .**Methods:** We followed the recurrences at the level of : the vaginal stump, at the level of the remaining paracolpium, in the iliac fossae and in the peri-aortocaval fossae and also in the peritoneum of the pelvic cavity . In the First Clinic of General Surgery and Surgical Oncology, a clinic with 70 hospital beds, of the Bucharest Oncology Institute, in Bucharest, Romania, in a 5 year time interval (1/01/2012-31/12/2017), we studied the percent of cancer recurrence after the standardized oncological surgical techniques in pelvic gynecologic cancers, performed by general surgeons specialized in surgical oncology. **Results:** Out of the total of 2100 patients operated on with the radical oncology techniques for cervical cancer, ovarian cancer and cancer of the uterine corpus during a period of 5 years, the recurrences encountered were around 20%, out of which 5% suffered a surgical intervention in our clinic for the excision of the tumour and, therefore, we had the possibility to document the cases. **Conclusions:** The authors consider that the recurrence rate encountered puts the techniques of radical surgery in the area of the preferred interventions, still remaining nowadays as the gold standard in the neoplasms of the pelvic cavity. The improvement of the recurrence rate -taking into account that this rate has decreased significantly over the years - cannot be the result of better surgery than it was 50-60 years ago, as the technique surgically speaking has remained the same, therefore, the progress must be due to improvement in chemo- and radiotherapy techniques. Nevertheless, the operative techniques, old as they might be, can be, and still are, very useful in the armamentarium used against pelvic cancers.



OP1-411

GROWING TERATOMA SYNDROME FOLLOWING TREATMENT FOR IMMATURE TERATOMA OF OVARY – A CASE REPORT

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Problem statement: Growing teratoma syndrome consists of enlarging metastatic masses arising during or after chemotherapy for a non-seminomatous tumours of testes/malignant ovarian germ cell tumors with teratomatous element, with normal serum levels of alpha-fetoprotein and human chorionic gonadotropin. The surgical excision of the metastatic masses confirms the presence of only mature teratomatous element. The preferred treatment is complete surgical resection because teratomas are resistant to chemotherapy and radiation therapy. **Methods:** We report the case of a young women with Growing Teratoma Syndrome following treatment for immature teratoma by surgery and chemotherapy. **Results:** 18 year old women, gravida 0, healthy, was evaluated for abdominal pain in the right iliac fossa with 3 weeks of evolution. At the physical examination it was found a soft and depressible abdomen, a pelvic mass that extends up to 4 cm below the umbilicus. Ultrasound scan and CT showed heterogenic solid pelvic mass with 10x9 cm of diameter slightly vascularized, positioned anterior and superior to the uterus admitting the left ovary as starting point, normal right ovary, without peritoneal effusion. Serum alpha-fetoprotein (AFP) was 26226 IU/ml and serum lactate dehydrogenase (LDH) was 294 IU/L. Other tumor markers were normal. She underwent hysterectomy and left salpingo-oophorectomy, infracolic omentectomy, bilateral pelvic lymphadenectomy and biopsy of paraaortic ganglia and adenomegaly. Absence of residual disease was observed at the end of the surgery. Histopathology confirmed a grade III immature teratoma without mental metastases or lymphatic invasion and she received adjuvant chemotherapy with bleomycin, etoposide, and cisplatin. After chemotherapy, positron emission tomograph (PET) and magnetic resonance images revealed a supravescical and near left ovary deposit suspected of metastatic disease. She underwent an excision of deposits. Histological diagnosis of the surgically resected specimens was of a mature teratoma. **Conclusion:** Growing teratoma syndrome is a rare outcome following treatment of malignant germ cell tumors. The diagnosis is confirmed by the exclusive presence of mature teratomatous element in the resected specimen. Though surgery is curative, these patients can also be safely followed-up in a majority of cases, with a favorable long term prognosis.

OP1-412

PRIMARY CYTOREDUCTIVE SURGERY OR NEOADJUVANT CHEMOTHERAPY AND INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN EPITHELIAL CANCER - PRELIMINARY RESULTS IN A SERIES OF 298 PATIENTS

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Ovarian cancer is the fifth most common cancer in women and the fifth leading cause of cancer death in women. Approximately 90% of ovarian primary malignancies have epithelial origin (carcinomas), and 70% of patients with ovarian epithelial cancers present with advanced stages, which raises major therapeutic problems. Advanced ovarian epithelial cancer (AOEC) treatment pillars are surgery and chemotherapy. Surgical treatment to achieve optimal cytoreduction (macroscopic residual tumors \leq 1cm) followed by adjuvant chemotherapy (AC) is the current standard in AOEC. Given that preoperative and/or intraoperative

explorations indicate low chances of achieving optimal cytoreduction, the benefits of cytoreductive surgery are diminished and/or uncertain. In these situations, performing a biopsy, preferably laparoscopic, followed by neoadjuvant chemotherapy (NAC) and surgical treatment with intention of R0/optimal cytoreduction is a treatment alternative that exposes the patient to lower surgical risks. **Material and method:** We performed a retrospective study on a group of 298 patients (PT) operated between 2007 and 2015 in the 1st Department of General and Oncological Surgery, Bucharest, "Al Trestioreanu" Institute of Oncology, of which in 82 PT were conducted biopsy interventions followed by NAC. We have examined each case in terms of the therapeutic sequence - primary cytoreductive surgery (PCS) + AC or biopsy + NAC + cytoreductive surgery (interval debulking surgery IDS), stage, histopathological type, degree of differentiation, extent of surgery and its complications. We evaluated the rate of R0 resections, overall survival (OS) and progression-free survival. **Results:** Depending on the maximum size of postoperative residual tumors we obtained resections: R0 to 70 PT (23.5%) of which 56 with PCS + AC and 14 with biopsy + NAC + IDS; \leq 1cm to 86 PT of which 60 with PCS + AC and 26 with biopsy + NAC + IDS; 1cm to 142 PT of which 101 with PCS + AC and 41 with biopsy + NAC + IDS. **Conclusions:** In patients with AOEC with low chances of achieving optimal cytoreduction, biopsy + NAC + IDS provides the possibility of a R0 resection at 17.1% of PT, with a risk of surgical sequelae considerably lower.

OP1-413

INTRODUCTION AND EVALUATION OF A SIMPLEST AND FASTEST CERVICAL CANCER SCREENING TECHNOLOGY FOR RESOURCES LIMITED AREA

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Early HPV screening and treatment of precancerous lesions is known to be highly effective in drop of cervical cancer death rate. However, HPV infection is still a global issue, especially in poor resources area, even though there are many HPV screening technologies available. The main reason is that sample treatment to extract DNA for HPV detection is very expensive, time consuming and complicated, not to mention complicated expensive equipment required for HPV detection that limits the HPV screening globally. In contrast, AmpFire HPV technology has the simplest sample process (Atila BioSystems, an isothermal amplification to detect all 15 high risk HPV in a single tube reaction and simultaneously genotype HPV 16 and HPV 18, plus an internal control). It doesn't require extracting DNA, simply heats to lyse the samples and then it is ready for detection. In addition, amplification is extremely fast (40 minutes). AmpFire HPV can be finished within an hour from sample to answer (10 minutes heating). The simplicity and speed of AmpFire HPV assay will be a great fit for poor resources area for global HPV screening. **Objective:** to evaluate the agreement of HPV detection between AmpFire HPV test and HC2 and their performance for HPV screening. **Methods:** A total of 80 patients samples were studied (samples collected in ThinPrep solution by **Lehay Clinic**, Burlington, MA). The AmpFire assay detects HPV virus by centrifuging 1ml ThinPrep sample solution, discharging the supernatant and then, the cell pellets were heat treated in a Atila lyse buffer for 10 minutes without DNA extraction. 2ul lysed simple was mixed with reaction solution for real time fluorescent detection in an hour. HC2 detection was done by Lehay Clinic following manufacturer's instruction. **Results:** Comparing HPV results of Ampfire HPV to HC2, amount the 80 samples, 78 samples are agreed with each other (56 positive samples and 22 negative samples). One sample AmpFire is positive, but HC2 is called negative with cutoff value at 0.62 that is larger than other reported positive cutoff value at 0.2. The other disagreement sample detected by AmpFire as negative, but HC2



report as positive without reporting cutoff value from Lehay Clinic. The %OA (overall agreement) is 97.5%. %PA (positive agreement) was 98.2, %NA (negative agreement) 95.5%. **Conclusions:** The Ampfire HPV assay performed equally well as HC2. Ampfire HPV assay did not require DNA extraction with very simple sample process and yielded results rapidly within an hour.

OP1-414

EFFECTS OF ELECTRIC FIELD ON ENDOMETRIAL ADENOCARCINOMA CELLS AND AUTOPHAGY ACTIVITIES

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Problem statement: Endometrial cancer is a group of epithelial malignancies that originate in the endometrium. It is one of the three most common malignancies in the female genitalia. In recent years, although the level treatment has improved, but the treatment after tumor metastasis recurrence is poor. To understand and use cell electrophysiological pathology may contribute to the adjuvant treatment of the tumor cells. The invasion and metastasis of tumor cells tend to transfer electricity, also affect the blood circulation of cancer cells. Understanding and controlling the biological variability of these electrical phenomena will be important to improve this treatment. Autophagy is also known as type II cell death, abnormal cell autophagy leads to the appearance of cancer cells. Autophagy can not only block the induction of apoptosis by inhibiting the activation of apoptosis-associated caspase which could reduce cellular injury, but also help to induce apoptosis. **Methods:** we selected ishikawa cells of the endometrial carcinoma cell line to be stimulated with electric field(EF) by 200 mV/mm for 4h-24h. We reported that cell morphology, directional migration and permutation induced by EF occur in obvious change comparison with normal cultured cells by microscopy imaging system. We found that the EF has an effect on the factors associated with autophagy in endometrial cancer cells. The cells stimulated by EF were collected at different time points, which protein extraction using protein extraction kit, getting the expression of different levels of autophagy factors (P62, beclin-1, LC3, ATG5/7) for Western blot analysis to obtain the protein relative expression compared to the gray value of the reference gene. **Result:** The results showed that under the EF intensity of 200 mV/mm, the factors of autophagy pathways were significantly changed when the cells were selected at 0h, 0.5h, 1h, 2h and 4h respectively, especially in P62 and ATG series. **Conclusions:** As an important physical signal, EF may play an important role in endometrial tumor cells. The increase of autophagic pathway-related factors (ATG5/7, etc.) induced by EF may promote the formation of autophagosome by phagocytic sequestration to affect autophagy.

OP1-415

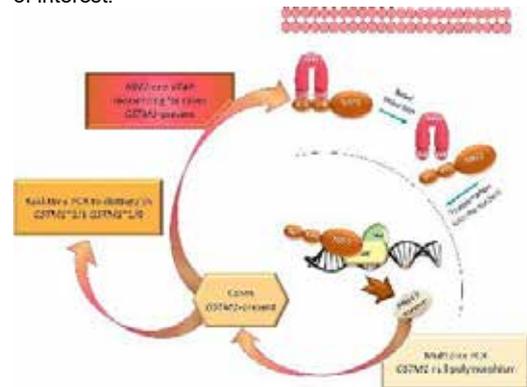
PROGNOSIS OF HORMONE-DEPENDENT BREAST CANCER SEEMS TO BE INFLUENCED BY KEAP1, NRF2 AND GSTM1 GENETIC POLYMORPHISMS

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Problem statement: Influence of Glutathione S-transferase Mu1 (GSTM1) has long been studied in breast cancer and *GSTM1* null genotype was correlated with breast cancer risk. Nuclear factor-erythroid 2-related factor-2 (NRF2) is a transcription factor that forms a complex with Kelch-like ECH-associated protein-1 (KEAP1), NRF2 negative regulator. Recent studies have demonstrated that expression of these proteins is deregulated in

several human malignancies. Thus, in the present study we aim to distinguish *GSTM1* heterozygous from wild type genotype in breast cancer patients and evaluate the presence and clinical significance of *NRF2* and *KEAP1* polymorphisms, alone or in association, with breast cancer prognosis, in cases confirmed to have *GSTM1*-present genotype. **Methods:** Study population consisted in 33 patients diagnosed with breast cancer. Genomic DNA was extracted and *GSTM1* was genotyped through multiplex PCR and gene dose was evaluated through real-time PCR. All cases *GSTM1*-present were sequenced through Sanger sequencing for specific regions of *NRF2* and *KEAP1*. Genotyping and clinicopathological data were correlated and statistical analysis was performed using SPSS. **Results:** *GSTM1* wild type was identified in 1 case and 16 cases were identified as heterozygous, these data were correlated with Human Epidermal growth factor Receptor 2 (HER2) status (p-value=0.032). We also verified that most cancers diagnosed at younger ages had the presence of *KEAP1* and/or *NRF2* polymorphisms. The association of *GSTM1* with rs35652124 and with rs6721961 also seems to be associated with HER2 status (p=0.036). **Conclusion:** Our results suggest that *GSTM1**1/0 genotype and the cumulative presence of at least one allele mutated in *KEAP1* and/or *NRF2* polymorphisms might be associated with worse prognosis for breast cancer patients. **Conflict of Interest:** The authors declare that they have no conflict of interest.



OP1-501

THE ASSOCIATION BETWEEN BLOOD TYPE GROUP AND EARLY POSTPARTUM HEMORRHAGE

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The most common cause of early postpartum hemorrhage is uterine atony, but coagulation disorders can also lead to heavy bleeding. Many studies have reported that ABO blood type system has an important effect on hemostasis, mainly by determining the level of VWF and indirectly determining the level of factor VIII in the blood. A, B and AB blood group individuals have VWF levels approximately 25-30% higher than O subjects. While a number of studies have analyzed the relationship between ABO blood groups and vascular thrombosis, only a few studies have been published on the association between ABO blood groups and hemorrhagic disorders. The aim of this study was to explore whether blood type O is associated with an increased risk for early postpartum hemorrhage compared to the other blood groups. **METHODS:** Data were collected for women who gave birth at Carmel Medical Center in Haifa between December 1, 2014 and March 3, 2016. Women were categorized according to blood type as O and non-O blood groups. The study included women at the age of 20-45 who gave birth at 34-42 weeks of gestation. Women with known coagulation disorders, unknown blood type and intrauterine fetal death were all excluded. The primary outcomes were defined as early postpartum

hemorrhage and blood transfusion. The comparison of categorical variables was done using the χ^2 or Fischer exact test, whereas the comparison of the continuous variables was done using student's t-test or ANOVA. The relevant data were further processed using a stepwise logistic regression model. **P RESULTS:** 4,516 women were included in the study, of which 1,594 (35.3%) were found to have blood type O. After multivariate analysis, blood type of the parturient was not associated with an increased risk for early postpartum hemorrhage and/or with packed red cells transfusion (OR 1.25, 95% CI 0.847-1.84, P = 0.26). There was also no association between the Rh blood group (positive/ negative) and the risk for developing postpartum hemorrhage (OR 0.97, 95% CI 0.44-1.4, P = 0.422). **CONCLUSIONS:** Blood type O is not associated with an increased risk for early postpartum hemorrhage or for blood transfusion.

OP1-502

AN UNUSUAL CAUSE OF ABDOMINAL PAIN IN A PATIENT WITH PLACENTA PRAEVIA

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Abdominal pain during pregnancy is common and accounts for a large number of hospital admissions. Ovarian vein thrombosis only occurs in 0.05% of pregnancies that result in live birth, and hence is often not suspected as a cause of an acute abdomen during this time. Classically it occurs after delivery but can very rarely present before and mimic a surgical abdomen. Several theories have been proposed to explain its aetiology, including venous stasis or damage, endometritis, and increased circulation of clotting factors. The case we present is of a 28 year old lady in her second pregnancy who was admitted at 33 weeks with severe abdominal pain, radiating down both legs and which did not improve with simple analgesia. Earlier sonography had revealed that the placenta was overlying the cervical os and was also suspected to be morbidly adherent. Multiple investigations were carried out, including blood tests and sonography of the abdomen and pelvis; but a diagnosis could not be reached. The patient had undergone an appendectomy and a cholecystectomy some years before and so these surgical causes for pain could be excluded. Finally, after a few days of investigations an MRI was carried out which revealed bilateral ovarian vein thrombosis. There is no consensus over treatment of this rare complication in pregnancy. In this case the decision of whether to anticoagulate was made even more difficult by the fact that the patient was at high risk of bleeding due to her placenta praevia. After consulting with the haematologists, it was decided to anticoagulate with intravenous unfractionated heparin until the thromboses resolved. A repeat MRI after 8 days confirmed resolution and the patient was switched to subcutaneous treatment until the 36th week, when a decision was taken for elective caesarean section. This was done after prophylactic occlusion of the uterine arteries under fluoroscopic guidance by the interventional radiologists. The balloons were inflated at the start of the procedure so the blood loss was kept to a minimum. The patient made an uneventful recovery.

OP1-503

THE EVALUATION OF THE FIRST-TRIMESTER BIOCHEMICAL PARAMETERS OF COMBINED ANEUPLOIDY SCREENING TEST IN PREGNANT WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS)

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Problem Statement: The maternal serum levels of pregnancy-associated plasma protein-A (PAPP-A) and free β - human chorionic gonadotropin (β -h CG) are being used as a biochemical markers to screen pregnancies with aneuploid fetuses. The serum concentrations of both molecules are related with decidualization and placentation process. Endothelial damage and impaired decidual trophoblast invasion were detected in pregnancies with polycystic ovary syndrome (PCOS). Recent studies suggested significant alterations in serum concentrations of PAPP-A and β -h CG in pregnant women with PCOS. The aim of this study was to evaluate the effect of polycystic ovarian syndrome on the biochemical components of first trimester combined aneuploidy screening test. **Methods:** A prospective case-control study was conducted on 489 women with singleton pregnancy in the first trimester (11⁺⁰-13⁺⁶weeks) at an academic tertiary care center between March 2014 and April 2017. One hundred and twenty four women who met Rotterdam criteria for PCOS before pregnancy constituted the study group and 365 women were with proven absence of PCOS formed the control group. Maternal PAPP-A, free β -h CG, and fetal nuchal translucency (NT) were measured and compared between the both groups. **Results:** The data regarding to baseline characteristics including gestational and maternal age, gravity, parity, maternal weight, and BMI were similar between two groups. In pregnant women with PCOS, the multiple median (MOM) levels of serum PAPP-A were significantly decreased when compared with those of the control group ($p=0.02$). No statistically significant differences in terms of the multiple median (MOM) levels of serum free β -h CG and NT measurements were detected between the PCOS group and the control group ($p=0.213$, $p=0.157$, respectively). **Conclusions:** The data suggested that PCOS was associated with low serum concentration of first trimester PAPP-A. The levels of serum free β -h CG were not affected by maternal PCOS. Further data from larger studies are needed to suggest the readjustment of PAPP-A during software calculation for risk analysis. There are no conflicts of interest **Keywords:** Polycystic ovarian syndrome, PAPP-A, free β -h CG, First-trimester screening test, Aneuploidy

OP1-504

PERINATAL OUTCOMES IN PREGNANCIES AFTER ADENOMYOMECTOMY WITH TOUA, IN A SINGLE INSTITUTE.

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Problem statement: The aim of study is to evaluate fetal outcomes in pregnancy after adenomyomectomy with TOUA (Transient occlusion of uterine arteries). **Material and Methods:** Between May 2011 and Oct. 2017, 26 cases of conception was analyzed, who have received adenomyomectomy with TOUA by YSK in a single institute. The analytic parameters include birth weight, abortion rate, amniotic fluid index, Fetal growth restriction, Apgar score, and fetal anomaly. The study was analyzed retrospectively by medical records. **Results:** Among 26 conceptions eleven cases were in pregnant and the other fifteen cases were delivered by cesarean delivery at until March 2018. The number of abortion was 3 cases. All were missed abortions in the first trimester and two abortions were occurred in one woman, repeatedly. There was no case of fetal growth restriction and no case of oligohydramnios during antenatal care. No fetal anomaly has been detected. There was no case of placenta abruption. Six among fifteen delivery cases had admitted to the hospital for managing preterm labor. The mean time of hospital staying due to preterm labor was 59 days (5 – 94, SD 36.4). The Mean birth weight was 2780 gram (1480-3750, SD 641) and the number of preterm



birth was six, who were admitted to NICU (neonatal ICU) not because of neonatal complications but for prematurity care. All neonates were well-being and discharged without significant complications. Apgar score of fifteen babies was mostly within normal range except in one case, Apgar score at 5 minute was below 7. However, the baby was recovered in ten minutes without long-term adverse outcomes. **Conclusion:** Except preterm birth, neonatal adverse outcome has not been found in this study and feto-uterine environment after adenomyomectomy with TOUA might be tolerable and safe.

OP1-505

SECOND TRIMESTER ULTRASOUND - INCREASING ERGONOMICS AND EFFICIENCY WITH A NEW EXAMINATION TABLE DESIGN

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Problem statement: The aim of the present project was to contribute with solutions to provide increased comfort and relaxation of the patient in an outpatient maternal ultrasound setting whilst retaining or improving ergonomics and efficiency for the sonographer. **Methods:** A prototype ultrasound examination table with heating in the upholster and removable side panels was constructed. Patients (n=70) and sonographers participated in an anonymous non-randomised survey with questionnaires concerning the experience of the examination table after a second trimester pregnancy ultrasound examination. **Results:** In comparison with a traditional examination table, the prototype was not rated higher in comfort or relaxation by the patients. However, sonographers rated it more maneuverable, expedient and ergonomic whilst increasing ease of conduct and reducing the average duration of the examination. **Conclusion:** An improved design of an examination table with removable side panels and internal heating of shows potential to improve sonographers' working conditions and reduce examination durations. Although at a higher purchase price than a traditional examination table, this prototype could be made economically viable by increasing efficiency in an outpatient ultrasound clinic. The authors have no conflicts of interest to declare.

OP1-506

FERTILITY AND PREGNANCY OUTCOMES IN PATIENTS WITH UTERINE ADENOMYOSIS, WHO HAVE RECEIVED ADENOMYOMECTOMY WITH TOUA IN A SINGLE INSTITUTE

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Problem statement: The aim of study is to evaluate fertility and pregnancy outcomes in patients who have received adenomyomectomy with TOUA (Transient occlusion of uterine arteries). **Material and Methods:** Between May 2011 and Oct. 2017, 397 patients was analyzed, who have received adenomyomectomy with TOUA by a single surgeon, YS Kwon, in a single institute. The analytic parameters included placental abnormality, Gestational age at delivery, contractility of uterus during Cesarean delivery, type of conception and antenatal care findings of pregnant women. The study was analyzed retrospectively by medical records. **Results:** Twenty-six women consisted of 12 cases of natural conception and 14 cases of ART (IVF) until March 2018. Among the natural conception cases, 3 cases were the patient who received laparoscopic adenomyomectomy. Mean age of women receiving of

adenomyomectomy was 35.4 years old (30-43, SD=3.1) and mean age when delivery was 37.4 years old (32-45, SD=3.0). Parity before adenomyomectomy was 0.33 (0-2, SD= 0.62). Interval between adenomyomectomy and delivery was mean 648 days (120-1287, SD=391.9). All were delivered by cesarean section. Mean gestational age at delivery was 37.3 weeks (28.6-39.4 SD=3.1). Placental abnormality was found in 4 cases, which included two accreta cases and two previa cases. However, there was no need of Cesarean hysterectomy or intervention such as uterine artery embolization due to postpartum hemorrhage. The uterine contraction was well in all fifteen cases without atonic findings after expulsion of placenta during cesarean delivery. There was no case of uterine rupture during pregnancy. **Conclusion:** Although there is limitation of study analysis because of small number of cases, deliveries after adenomyomectomy with TOUA did not significantly increase maternal and neonatal adverse outcomes. Intensive antenatal care would prevent complications during pregnancy.

OP1-507

SUCCESSFUL OUTCOME OF HEPATIC ADENOMA RUPTURE ON INTRACYTOPLASMIC SPERM INJECTION RELATED PREGNANCY

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Problem statement: The authors report a successful outcome on a spontaneously rupture large hepatic adenoma on an intracytoplasmic sperm injection related pregnancy. The natural history of these lesions during pregnancy is incompletely understood and resection should be considered if worsening symptoms or the clinical concern for rupture. It is believed that the female sex hormones, particularly oestrogen, have an influence on development and growth. **Methods / Case Report:** 36 years old female with a 7 year infertility history due to male factor underwent a 3rd In Vitro Fertilization (IVF) cycle with previous endometrium scratching. Double embryo transfer on day 3 (Grade A/A) was performed. Uneventful pregnancy. **Results:** At 37th weeks gestation after complaining of intermittent right upper quadrant discomfort, admitted on obstetrics emergency room. After a pathological cardiotocography, emergency fetal extraction was decided. During caesarean section, moderate hemoperitoneum was observed as well as hematic amniotic fluid and an abruptio placentae was detected. Healthy baby boy with 2870g was extracted, with Apgar score of 9, 10, 10 at the 1st, 5th and 10th minute. Fetal umbilical vein pH was 7.40. Further abdominal investigation revealed a large 10 cm hepatic adenoma rupture. A hepatic resection on the 5th segment was performed. **Conclusions:** There is little available literature describing the outcome of liver adenoma resection during pregnancy. Both pregnancy and hormonal therapy, including controlled ovarian stimulation drugs, have been associated with adenoma enlargement. Spontaneous rupture is the complication most feared because this is associated with a mortality rate approaching 80%. **Disclosure of interest:** The authors report no potential conflict of interest to disclose. Keywords infertility, assisted reproductive technology, hepatic adenoma

OP1-508

PERIPHERAL NATURAL KILLER CELLS IN INFERTILE WOMEN: CLINICAL PREGNANCY RATES AND MISCARRIAGE INCIDENCE

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Problem statement: Natural killer (NK) cells are crucial for establishment and maintenance of pregnancy. Nevertheless, elevated numbers of peripheral NK cells are supposed to have adverse effect on implantation and pregnancy outcome. This statement should be taken with caution, as more clinical and scientific data are needed to confirm it. We present a retrospective analysis of NK cell percentage of lymphocytes and count in peripheral blood of infertile women. **Methods:** The percentage of lymphocytes and absolute count ($\times 10^6/L$) of NK cells (CD56⁺CD16⁺) assessed by Fluorescence-activated cell sorting (FACS) in peripheral blood of totally 200 women from infertile couples were analyzed. As 32 (16%) of the couples were excluded because of male factor infertility, 168 women were included in the study and divided into two groups: ≤ 35 years ($n=126$) and > 35 years ($n=42$). According to NK cell percentage, patients were divided into subgroups: 8, 8-12, 13-19, $\geq 20\%$. According to NK cell count, the subgroups were: 6/L. Clinical pregnancy rates (CPR) and miscarriage incidence in the groups were analyzed and compared to NK cells percentage and absolute count. **Results:** In the groups ≤ 35 and > 35 years the mean NK cell percentage and count for the women who achieved pregnancy after natural conception or assisted reproductive technology (ART) treatment, who didn't achieve pregnancy and who miscarried are listed in Table 1. Regarding the miscarriage history of the patients, the mean NK percentage and count for the two age groups are also presented in Table 1. No statistical significance (Mann-Whitney U-test) was obtained. There was not statistically significant difference in the CPR and miscarriage incidence according to NK percentage or count (Chi-square test) between the cited subgroups: NK cell percentage 8, 8-12, 13-19, $\geq 20\%$, NK cell count 6/L in none of the age groups. **Conclusion:** In the present study we report the mean values for peripheral NK cell percentage and count in infertile patients in correlation to the CPR and spontaneous abortion incidence. Our results demonstrate that in women with reproductive problems these two immune parameters could not be related to CPR or miscarriage prevalence.

Table 1

≤ 35 years	Patients (n)	NK %* \pm SD	NK count** \pm SD
≤ 1 miscarriages	40	14.2 \pm 6	336.2 \pm 193.6
No history of miscarriage	86	14.1 \pm 5.8	302.8 \pm 148
Total	126		
Pregnancy	76	14.5 \pm 5.9	327.2 \pm 165.8
No pregnancy	36	13.3 \pm 5.9	277.5 \pm 124.7
Pregnancy Miscarriage	10	14.4 \pm 8.4	384.3 \pm 257.8
Total	122		
> 35 years			
≤ 1 miscarriages	19	14.8 \pm 5.2	314.8 \pm 117.4
No history of miscarriage	23	16.1 \pm 7.9	339.9 \pm 178
Total	42		
Pregnancy	20	16.6 \pm 7.2	354.1 \pm 167.4
No pregnancy	18	13.1 \pm 5.9	282.1 \pm 134.5
Pregnancy Miscarriage	2	19.5 \pm 3.5	451.0 \pm 118.8
Total	40		

* %: percentage of lymphocytes
 ** count: $\times 10^6/L$

OP1-509

AN ANALYSIS OF PREGNANCY PERCEPTION OF PREGNANT WOMEN IN TERMS OF STRESS, DEMOGRAPHIC AND OBSTETRIC CHARACTERISTICS

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Problem statement: This study was conducted to examine the pregnancy perception of pregnant women in terms of stress, demographic and obstetric characteristics. **Methods:** The cross-sectional study included 397 pregnant women who applied to the Gynecology Department of the Faculty of Medicine at a foundation university in Istanbul between March-July 2018. Data were obtained with Introductory Information Form, Self-Perception of Pregnants Scale (SPPS) and Prenatal Distress Questionnaire (PDQ). Ethical approval and written consent of the participants were obtained. **Results:** The majority of women were between the ages of 18-35 years (82.9%), 83.4% were at least junior high school graduates, 75.6% were housewives, 36.8% were primigravida, 87.9% were in the 2nd or 3rd trimester, 45.1% had given their last birth by cesarean section and 68.3% had planned pregnancy. The average SPPS-Maternity sub-dimension score was 25,82 \pm 2,87; The average of SPPS-Body sub-dimension score was 9,41 \pm 3,67; The average of PDQ score was 10,26 \pm 5,18. PDQ score had a significant negative correlation with SPPS Maternity perception score ($r=0.260, p0.001$), and positive correlation with the SPPS-Body perception score ($r=0.363, p0.001$). Socio-demographic characteristics of women didn't significantly affect the SPPS-Maternity and Body perception score ($p0.05$). However, situation of planned pregnancy ($z=3.155, p0.01$), giving last birth by cesarean section ($z=2.379, p0.05$) and having a harmonious relation with the spouse ($KW=52.536, p0.001$) ($z=2.386, p0.05$) had a positive effect, and the situation of having problems with the current pregnancy had a negative effect significantly. The average PDQ score of pregnant women with ≥ 3 children was significantly higher than other groups ($KW=10.384, p0.01$), while the average PDQ scores of pregnant women who had a planned pregnancy and had a harmonious relationship with their spouses were significantly lower. **Conclusion:** Maternal perception of the pregnant women was high, their body perception was positive and stress level was low. Maternity and body perception of pregnant women is affected negatively when the distress level of pregnant increases. Both distress levels and maternal and body perceptions of the pregnant women who got pregnant without planning, who were incompatible with their husbands and who had health problems were significantly affected negatively. The authors have no conflict of interest to disclose. **Keywords:** Pregnancy, Self-perception, Distress, Factors Affecting

OP1-510

GIANT CYSTADENOMA IN PREGNANCY: A LAPAROSCOPIC APPROACH

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Problem statement: A 25-year-old women, five weeks pregnant, with no prior medical history, addressed our emergency room complaining of pelvic pain. On physical examination she presented with a palpable abdominal mass from the pelvis to the inferior



border of the liver. On ultrasound we identified a gestational sac compatible with a five-week pregnancy and a right adnexal mass consisting of a unilocular cyst with no septa or papillary projections with approximately 18 centimetres in diameter. An abdominopelvic magnetic resonance was performed which confirmed the ultrasound findings. In the absence of acute symptoms, we opted for a conservative approach. At 18 weeks gestation we performed an exploratory laparoscopy with detection of a right ovary mass with a cyst like appearance of about 15 centimetres in diameter. Aspiration of the cystic fluid and atraumatic decapsulation with exteriorization of the right adnexa was then carried out. **Methods:** The aim of this presentation is to demonstrate a step-by-step video of the surgical technique applied in the treatment of large adnexal cysts in pregnancy. Therefore, we performed a video edition with the laparoscopic footage of the surgical intervention. **Results:** Laparoscopic cystectomy was performed, and operative time was about 60 minutes. No surgical complications were reported. Cytological and anatomopathological exam revealed a mucinous cystadenoma with no signs of malignancy. The pregnancy developed normally to term. **Conclusion:** About one to four percent of pregnancies are complicated by adnexal masses, most of which are benign cysts and regress in the first trimester. When they do not regress, surgical intervention is sometimes required. Laparoscopic approach in these situations is beneficial and preferable since there is less uterine manipulation and we avoid the creation of a large abdominal scar while the uterus is enlarging. **Disclosure statement:** The authors have nothing to disclose.

OP1-511

MATERNAL VITAMIN D DEFICIENCY INCREASES THE RISK OF GESTATIONAL DIABETES: A PROSPECTIVE STUDY

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Problem statement: Gestational diabetes mellitus (GDM) has been recognized as an important risk factor for poor pregnancy outcomes. Even though the mechanistic basis of GDM has not been completely understood, the evidence is accumulating for a role of vitamin D in maintaining normal glucose homeostasis. However, studies that prospectively examined the link between vitamin D deficiency and the development of GDM are limited. The aim of this study is to determine the association between maternal vitamin D serum levels in the first trimester of pregnancy and the risk of GDM. **Methods:** A prospective cohort study was performed including women with a singleton gestation who underwent first-trimester screening for aneuploidy at Alto Minho Local Healthcare Unit, Viana do Castelo, Portugal, between April and May 2018. Vitamin D serum levels were measured between 11 weeks 0 days and 13 weeks 6 days of gestation. GDM was diagnosed according to *International Association of the Diabetes and Pregnancy Study Groups* criteria. **Results:** Among 90 pregnant women included in this study, 11 (12.2%) were diagnosed with GDM. Vitamin D levels were significantly lower among GDM pregnant women (11.7±3.3 vs. 19.1±7.2, $p=0.001$). Vitamin level in first trimester was a predictor of GDM even after adjusting for maternal age, pregestational body mass index, pregestational weight, chronic hypertension and familial diabetes history (AOR=0.789; CI:0.671–0.928, $p=0.004$). **Conclusions:** Low maternal vitamin D levels during the first trimester was a predictor of GDM. More research in this area is warranted to elucidate further the role of vitamin D in GDM pathogenesis.

OP2-101

ENDOVASCULAR MANAGEMENT OF INTRAPARTUM ACCRETA: A USEFUL UTERUS-PRESERVING TECHNIQUE FOR FUTURE FERTILITY

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Problem statement: Abnormal placentation/aberrant implantation is a rare, life-threatening condition that occurs when the chorionic villi abnormally invade the myometrium due to the absence of the decidua. Our study was conducted to evaluate the efficacy of internal iliac arteries trans catheter embolization for control of intractable intra-partum hemorrhage. **Methods:** We report our experience in managing prospectively abnormal placentation using prophylactic balloon occlusion of the internal iliac arteries (IIAs) bilaterally in a case series of five patients. Between January 2012 to December 2014, all our patients had planned deliveries at term gestations and the IIAs were occluded with balloons. Consent forms were obtained from each patient before the procedure. **Results:** Embolization was performed by using Gelfoam through interventional radiology. The intraoperative findings were of placenta accreta, placenta increta, and placenta percreta. No histopathology examination was requested as hysterectomy was not performed in any case. No severe complications were observed. **Conclusion:** Through prophylactic Gelfoam- balloon occlusion of the IIAs, this management approach not only offered less blood loss compared to hysterectomy, but also preserving reproductive function. **KEY WORDS** Placenta Accreta; Balloon Occlusion; Interventional Radiology; Internal iliac arteries

OP2-102

EFFECT OF ANTENATAL EDUCATION AND COUNSELING TO FEAR OF CHILDBIRTH AND CHILDBIRTH ATTITUDES IN NULLIPAROUS PREGNANT WOMEN

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Problem Statement: Antenatal education is considered essential for pregnant women in many parts of the world. There have been various studies that show positive effect on pregnancy. The aim of this study was to determine the effect of education and counseling giving to nulliparous pregnant women during the third trimester regarding birth preparation and how to deal with childbirth pain on childbirth fear and fear of childbirth attitudes. **Methods:** This prospective randomized controlled intervention study was conducted between the dates September 2015 and October 2016 in Gulhane Training and Research Hospital, Department of Obstetrics and Gynecology. The sample of the study consisted of 132 nulliparous pregnant women between the 28-34th gestational weeks of whom 65 were in the intervention group and 67 were in the control group. The data were collected by using data collection form, The Wijma Delivery Expectancy/Experience Questionnaire Version A (WDEQ-A), The Wijma Delivery Expectancy /Experience Questionnaire Version B (WDEQ-B) and Childbirth Attitudes Questionnaire. Antenatal education and counseling via telephone was applied respectively after pre-test to intervention group. Post-intervention assessment was conducted at 38-40th gestational weeks and postnatal 1-2th days. Control group had no intervention. They applied pre-test and post-test same time with intervention group. Obtained data were evaluated by using frequency and percentage calculations, chi square test, Independent Sample t



Test, Mann-Whitney U, Kruskal Wallis, Wilcoxon t, and Mc Nemar Bowker tests. **Results:** There was statistically significant difference between intervention and control groups in terms of WDEQ-A ($Z=-5.034$; $p=0.001$), WDEQ-B ($Z=-8.951$; $p=0.001$), and Childbirth Attitudes Questionnaire ($Z=-5.663$; $p=0.001$) sum scores. **Conclusion:** Antenatal education and counseling to prepare childbirth and cope with pain of childbirth giving to nulliparous women have important effect to reduce fear of childbirth and negative attitudes towards fear of childbirth.

OP2-103

CONSENT IN CAESAREAN SECTION – ARE WE DOING IT RIGHT?

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Problem statement: The incidence of caesarean section (CS) is rising annually and is currently 27.5% worldwide¹. It is essential to obtain valid consent prior to CS after providing: accurate information on the procedure, alternative options, intended benefits and associated risks. The aim of this audit was to identify if current consenting practice in Aberdeen Maternity Hospital (AMH) meets the standards set by RCOG (Royal College of Obstetrics and Gynaecology) and NICE (National Institute for Health and Care Excellence). **Methods:** 100 women who underwent CS prior to the 01/05/2017 were identified retrospectively. All documentation and information on the consent form was collected and analysed. Results were presented to staff at the AMH audit meeting and emails and posters were used to communicate results. After a six week intervention period, another 100 women were identified and consent forms analysed as before. RCOG and NICE guidance was used as the gold standard for accurate completion of the form. Standards were set at 100% for patient demographics and patient/professional signature, printing and dating. Standards of 95% were set for proposed procedure, additional procedures, intended benefits, risks and additional information given. This allowed for cases of individual variation and clinical appropriateness. **Results:** Standards were not met in either cycle for any of the main outcomes measured. Standards ($\geq 95\%$) were met in three sub-sections for both cycles: documentation of risk of bleeding, infection and damage to the urinary tract. However improvements were seen between cycles with a ten-fold increase in documentation of possible hysterectomy, a five-fold increase in documentation of risks to future pregnancies and the complete removal of generic statements of risk e.g. "damage to nearby tissue" in cycle two. **Conclusion:** Despite a full audit cycle wide variation in consenting practise persists which does not meet RCOG and NICE standards. Further work is needed to improve the consenting process for both patients and staff. This may involve a patient satisfaction questionnaire, generation of a new form and enhanced distribution of audio/visual material. **References** NHS Digital. NHS Digital. *NHS Maternity Statistics, England; 2016-2017*

OP2-104

BLOOD LOSS, MASSIVE TRANSFUSION AND HEMOGLOBIN LEVELS IN PATIENTS UNDERGOING EMERGENCY PERIPARTAL HYSTERECTOMY AT A GERMAN TERTIARY PERINATAL CARE UNIT DURING THE LAST 13 YEARS

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Problem: Peripartum hysterectomy (PH) is an emergency procedure for managing life-threatening abnormal uterine bleeding and with its challenging character, this procedure leads to elevated maternal morbidity and mass transfusions. For an overview about

the average loss of blood as well as the blood transfusion behavior in these situations, we analyzed data from cases of PH performed in a German University Hospital in the last 13 years. **Methods:** At the tertiary care center of the Department of Gynecology and Obstetrics at the University Hospital Ulm 41 emergency PH were performed between 2004 and 2016. Recorded data from all patients were retrospectively analyzed regarding loss of blood, number of transfused blood products and hemoglobin levels before surgery and at time of discharge. **Results:** Ranging from 150 to 20000 ml, median loss of blood estimated by surgeons postoperatively was 4500 and significantly correlated with number of transfused red blood cell units ($r_s = 0.77$, $p = 0.001$) as well as total amount of transfused blood products ($r_s = 0.73$, $p = 0.001$). Hemoglobin levels at time of administration to and time of discharge from the hospital showed no significant correlations with number of transfused red blood cell units, or total amount of transfused blood products (all $p > 0.05$). Median total amount of blood products transfused was 6.9 l (range 0.6 – 32.7) with 11 packed red blood cells (range 0 – 55 products), 10 FFPs (range 1 – 43) and 2 platelet concentrates (range 0 – 16). There was a significant correlation with theatre time ($r_s = 0.40$, $p = 0.010$ and $r_s = 0.39$, $p = 0.011$, respectively), and with length of stay in ICU ($r_s = 0.42$, $p = 0.007$ and $r_s = 0.40$, $p = 0.009$, respectively) for both, the number of transfused red blood cell units and the total amount of transfused blood products. **Conclusion:** PH is also in the setting of a university hospital a high risk procedure often resulting in massive transfusions for excessive loss of blood. Preoperative risk assessment with stand-by of experienced teams and interdisciplinary availability is essential for adequate management of emergency PH.

OP2-105

EVALUATION OF PERIOPERATIVE PRACTICES ACCORDING TO EROS PROTOCOL IN ELECTIVE CESAREAN SURGERY

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This descriptive and prospective study was conducted to evaluate perioperative practices in elective cesarean operations according to the Enhanced Recovery in Obstetric Surgery (EROS) protocol. The sample consisted of 100 pregnant women. The data collection form consisted of descriptive characteristics and EROS protocol proposals. Each participant received preoperative information and counseling. No intestinal preparation and premedication was applied. Mean preoperative restriction time of solid food intake was 12.17 ± 3.37 hours, mean restriction time of oral fluid intake was 10.36 ± 2.85 hours. No woman was given high calorie drinks before surgery. Preoperative IV fluid therapy was performed in 4% of the women, preoperative LMWH was applied to 2%, all were treated with antibiotic prophylaxis after clamping the newborn's cord. Spinal anesthesia rate was 77%; general anesthesia rate, 23%. Average surgical incision length was 15.83 ± 0.81 cm. To prevent hypothermia, a heated mattress was used during the operation, and a warm air blower was used in the wake-up area for all women. 58% of women were treated with 1000 cc saline and 500 cc artificial colloid. Nasogastric tube and drain were not used. Only 5% were treated with LMWH, and all received a postoperative antibiotic dose. Postoperative mean time for starting oral fluid intake was 6.18 ± 2.0 hours, mean time for starting solid food intake was 16.46 ± 5.85 hours, mean time for starting breastfeeding was 1.56 ± 1.95 hours, mean mobilization time was 6.41 ± 1.68 hours, mean urinary catheter removal time was 7.99 ± 2.86 hours. All were given 2000 cc crystalloids. Only 2% had nausea. 96% required analgesia and 91% of these were administered opioid-free analgesics. After written and oral discharge training, all were discharged on the second postoperative day. None were readmission within 40 days. It is recommended that the minimal



interruption of oral intake should be calculated according to the time of the cesarean section. The high calorie drinks before the operation can be evaluated. In the postoperative period, women generally wait for the release of gas before oral intake, but this can be reassessed for those without complications. Necessary arrangements can be made for the initiation of breastfeeding in the operating room for women with spinal anesthesia.

OP2-106

DOES INTRAHEPATIC CHOLESTASIS OF PREGNANCY PRESENT DIFFERENTLY IN IN VITRO FERTILIZATION VERSUS SPONTANEOUS PREGNANCIES?

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Objective: Intrahepatic cholestasis of pregnancy (ICP) is an uncommon unique hepatic disorder in pregnancy. It is characterized by pruritus accompanied by elevated total serum bile acids and/or aminotransferase levels, in the absence of diseases that may produce similar laboratory findings and symptoms. The etiology of this disorder is complex and appears to be associated with the cholestatic effect of reproductive hormones. Therefore, this study aimed to explore the impact of IVF on ICP progress.

Methods: This retrospective cohort study included all women referred to Carmel Medical Center due to ICP between the years 2010 to July 2018. ICP was defined as presence of pruritus in the absence of skin rash, in conjunction with increased level of serum bile acids (i.e. above 8 $\mu\text{mol/L}$) in fasting women, and/or increased alanine transaminase (ALT, above 40 U/L). IVF pregnancies were compared to the remaining cohort in terms of week of ICP diagnosis, bile acid levels and various obstetric characteristics.

Results: Overall, 85 pregnancies with ICP were included. Of these, 19 (22.4%) were conceived by IVF. In this group, ICP was diagnosed at significantly earlier gestational age -33.5 ± 2.5 weeks compared to 35.0 ± 2.6 weeks in the remaining cohort ($p=0.0307$). No noticeable differences were found between IVF vs. non-IVF pregnancies in terms of bile acids level (39.4 ± 38.3 vs. 27.9 ± 21.5 $\mu\text{mol/L}$, respectively, $p=0.1469$) or liver enzyme levels (ALT 125.1 ± 125.0 vs. 123.9 ± 106.0 U/L, $p=0.969$). Patients conceived by IVF delivered at an earlier age (35.0 ± 2.6 vs. 36.3 ± 1.8 weeks, $p=0.0487$, respectively) and yielded a significantly higher rate of cesarean sections ($13=68.4\%$ vs. $22=32.4\%$, $p=0.0074$), but also a higher rate of twin pregnancies ($11=57.9\%$ vs. $6=8.9\%$, $p=0.0001$). **Conclusion:** In this study we found that ICP was diagnosed at significantly earlier gestational age in IVF group than in spontaneous pregnancies. Earlier week of delivery and higher rate of cesarean sections in IVF cohort are probably related to a higher percentage of multiple pregnancies. Large-scale prospective studies are warranted to better define the relationship between IVF and cholestasis of pregnancy, and to clarify its clinical implications.

OP2-107

TRAUMA, VIOLENCE, AND BIRTH: COMMUNION AND AGENCY IN NARRATIVES OF DIVERSE BIRTH EXPERIENCES

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Problem Statement: Traumatic birth experiences represent 34% of all birth experiences in the United States. Thought birth and labor related factors are assumed to be the cause of traumatic experiences, most mothers attribute their trauma to feelings of undermined agency and a lack of communion with caregivers during labor and delivery, as well as during the vulnerable post-partum experience. The psychological and physiological impacts of traumatic birth are known to interfere with the acute and chronic

well-being of the mother-baby dyad. **Objective:** To identify pathways of positive and negative agency and communion in original narrative accounts of diverse birth experiences. **Methods:** We analyzed birth narratives of 20 mothers using a phenomenological narrative analysis to map pathways of positive and negative birth experiences via acts of agency and communion. **Results:** Positive birth experiences were identified are critical for the long-term health and wellness of the mother-baby dyad. Positive birth experiences were characterized by pride in the functioning of one's maternal body, establishing closeness with their baby, positive interactions with caregiving authorities, and active engagement in all stages of birth. Negative birth experiences were characterized by a lack of autonomy over birth decisions, disrupted communion with one's caregivers, and experiences of physical and structural violence. **Conclusions:** Positive birth experiences are critical for promoting maternal psychological well-being, as well as facilitating a successful transition to early motherhood. Optimized birth experiences allow mothers to feel autonomy over their bodies and their decisions, as well as create positive, supportive encounters with caregiving authorities. Caregiving authorities should prioritize empowered decision-making as a strategy for preventing trauma during the birth experiences, as well as review protocols for best-practices that reduce psychological and physical maternal harm. Funding source: Co-funded by the College of Fine Arts, Humanities and Social Sciences and the Office of the Vice Chancellor for Research and Innovation: University of Massachusetts, Lowell (R50180000038539).

OP2-108

EFFECTS OF CORTICOSTEROIDS ON CARDIOVASCULAR FUNCTIN OF FETUSES WITH GROWTH RESTRICTED

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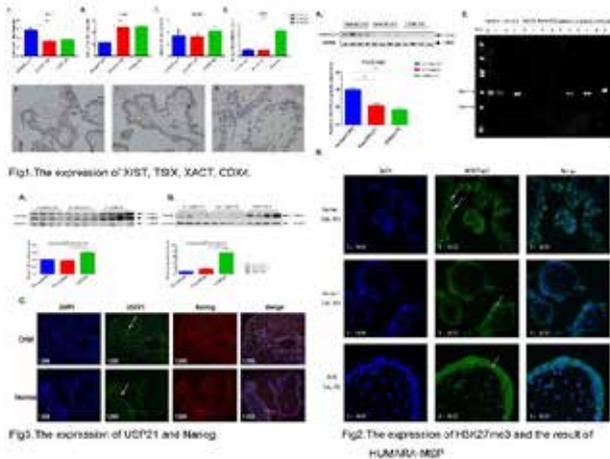
Objective: evaluation of cardiovascular effect of corticosteroids in growth restricted fetuses. **Method:** Our study was cohort study that was done from February 2014 to March 2017 in Hafez Hospital, Shiraz University of Medical Science, Iran. The pregnancies were singleton with GA 26 to 38 weeks which are complicated by IUGR, with permission to receive first doze of corticosteroids for induction of lung maturity. Fetal venous, arterial Dopplers, CPR & assessment of myocardial function (left & right) by calculating performance index (MPI) before then 24 hours after first doze of betamethasone is evaluated. Kolmogrov-Smirnov test approved normality of all the variables thereby we used paired T-test to examine the difference between before & after exposed to corticosteroids. **Results:** Eighteen pregnant women were participated in this study. The mean gestational age was 31.4 weeks (Range from 25 to 36). Paired T-test showed a significant decrease in right MPI (0.66 versus 0.6, $P=0.26$). In left, decrease in MPI was not significant (0.64 versus 0.59 $P=0.26$). Mean (SD) of UMA pulsatility index before and after corticosteroid exposure was $1.52(0.57)$ and $1.35(0.55)$ which was significantly different ($P=0.045$). Moreover, our results confirmed significant decrease in pulsatility index of MCA. There was no significant change in CPR & in pulsatility index Ductus venosus. **Conclusion:** In growth restricted fetus, corticosteroids cause vasodilation in fetus, It is which is leading to reduce afterload, increase cardiac output. It is reflected by significant decrease in right MPI. In contrast corticosteroids could improve fetal heart function & reduce the negative effects of IUGR. Decreasing UMA PI, give us the time to delay emergency termination and waiting to receive maximum effect of corticosteroids in long maturity.

OP2-109

LOSS OF X CHROMOSOME INACTIVATION IN MONOSPERMIC COMPLETE HYDATIDIFORM MOLES WITH 46, XX KARYOTYPE.

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Problem statement: Most of complete hydatidiform moles(CHMs) present an androgenetic nature of the nuclear genome. In normal female embryo, one of two X chromosomes is inactive. But the status of X chromosome inactivation(XCI) in monospermic CHMs remains unknown. **Methods:** 71 monospermic CHM tissues with 46, XX karyotype were collected. 74 normal female villi and 74 normal male villi were collected as controls. The expression of XCI markers (XIST, TSIX, and XACT) and a X-linked gene (CDX4) was detected by RT-PCR. Other XCI associated genes were also examined, including the methylation status of human androgen receptor gene(HUMARA) by methylation-specific PCR(MSP), and the expression of H3K27me3, USP21, and Nanog by Western blot and immunofluorescence, respectively. In addition, 126 CHMs and 63 normal female villous samples were collected for CDX4 immunohistochemical staining. **Results :** XIST RNA expression was significantly lower and TSIX RNA expression was significantly higher in monospermic CHMs than that in normal female villi (both P<0.01). The expressions of CDX4 mRNA in monospermic CHMs was elevated compared with normal (both P<0.01), and CDX4 protein expression was also higher than that in normal female villous samples (P<0.01). The expression of H3K27me3 was decreased in monospermic CHMs compared with normal female villi (P<0.01). The methylation pattern of HUMARA was lacked in monospermic CHMs. The expression of Nanog and USP21 protein in monospermic CHMs was higher than normal villi (both P<0.01). **Conclusion :** Both X chromosomes are active in monospermic CHMs with 46, XX karyotype, and the USP21-Nanog pathway may be involved in the disruption of XCI during this process.



The authors declare that they have no competing interests

OP2-110

INTRAPLACENTAL VILLOUS ARTERY DOPPLER AS AN INDEPENDENT PREDICTOR FOR PLACENTA MEDIATED DISEASE AND ITS COMPARISON WITH UTERINE ARTERY DOPPLER AND/OR PLACENTAL BIOCHEMICAL MARKERS: A PROSPECTIVE COHORT STUDY

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Objectives: To validate intraplacental villous artery (IPVA) Doppler, as a predictor for placenta-mediated diseases (PMDs) and to compare its predictive values with uterine artery (UtA) Doppler and placental biochemical markers. **Methods:** IPVA and UtA resistance indices (pulsatility and resistant indices (PI and RI)) were recorded at 18 - 24 weeks' gestation in a cohort of 117 women. The predictive value of the IPVA, UtA and placental biochemical markers were analyzed and compared between the PMD (the women who developed preeclampsia or intrauterine growth restriction) and non-PMD group (the women who remained healthy throughout the pregnancy and three months postpartum) using the receiver operating characteristic (ROC) curves. **Results:** 31 (26.5%) women developed PMDs (17 preeclampsia and 14 intrauterine growth restriction). IPVA PI was significantly higher in PMD group in comparison to non-PMD group (P=0.001). UtA PI and RI remained non-significant between the two groups (P=0.066, 0.104). IPVA PI sampled over all placenta (three main branches), and specifically in a central main stem villi showed strong association with PMDs in comparison to UtA (P=0.03, 0.001 vs 0.29). **Conclusions:** IPVA PI appears superior in a prediction of PMDs when compared to UtA PI or RI and to placental biomarkers. Nothing to disclose.

OP2-111

PREGNANCY AND BIRTH AT WOMAN BORN WITH GASTROSCHISIS

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Gastroschisis is one of the most common malformation of fetal abdominal wall. The mass of bowel that protrudes through defect of abdominal wall is not covered with membrane. It is necessary to do first surgical care right after the birth and for some children there will be more surgical interventions needed during the childhood. CASE REPORT: Expectant mother, age 29, was admitted to our hospital in 30. (29 + 1/7) week of her first pregnancy. She was admitted because of the ultrasound finding of intrauterine growth restriction of fetus, estimated weight was 825 grams, under 3. percentiles. From anamnesis we found out that expectant mother was born with gastroschisis, she was operated right after the birth when 12 cm of her bowel was removed. 39. day after her birth she had ileus and one more surgery was done and at the age of 12 reconstruction of anastomosis. The last surgery was in 2014. when our patient again had an ileus. From her childhood she was suffering from megaloblastic and sideropenic anemia, a short bowel syndrom and malabsorption syndrom. During her stay we gave her Dexamethasone for stimulation of maturation of fetal lungs. 8. day of her stay at our Clinic we did the ultrasound examination that showed the flow through the umbilical artery 0,77 with occasional absence of diastola and through middle cerebral artery 0,62. Medical consilium made a decision that expectant mother will have a C-section. Considering the anamnesis for the successful completion of pregnancy we needed multidisciplinary team- surgeon who reached the gravid uterus,

experienced obstetric and neonatologists team. We did the lower midline relaparotomy. The child was born at the gestational age of 30 + 2/7 weeks and it weighted 957 grams, Apgar 6 in the first minute and 8 in the fifth minute. Postoperative course of mother was neat, while the child is still at the intensive care unit and is progressing nicely. In our conclusion, we would like to highlight that during the surgical care of children born with gastroschisis we need to have in mind that someday they will be the future mothers.

OP2-112

THE CONCENTRATIONS OF PLACENTAL GROWTH FACTOR AND ENDOGLIN IN PREGNANCY COMPLICATED BY PRE-ECLAMPSIA

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Problem statement: Pre-eclampsia complicates about 5-10% of pregnancies and there is one of the most important causes of maternal and fetal/neonatal morbidity and mortality. The syndrome is the main cause of intrauterine growth retardation and iatrogenic prematurity. The aim of the study was to assess the role of Placental Growth Factor PLGF and soluble form of Endoglin sENG in the group of patients with pre-eclampsia and healthy pregnant women. **Methods:** The sera concentrations of PLGF and sENG were measured with the use of immune-enzymatic method. The study included 33 patients with pre-eclampsia and 44 healthy women in I, II and III trimesters of uncomplicated pregnancy. **Results:** The concentrations of PLGF were significantly lower in the group of patients with pre-eclampsia when compared to healthy pregnant women (median: 3,3 pg/ml vs. 19,8 pg/ml, p0,001). Moreover, in the group of patients with pre-eclampsia the concentrations of sENG were significantly higher when compared to healthy pregnant women (median: 11,47 ng/ml vs. 6,13 ng/ml, p0,001). In the group of patients with pre-eclampsia there were negative correlation between the concentrations of sENG and the concentrations of PLGF (R=-0,21). In the group of healthy pregnant women there was a negative correlation between the concentrations of sENG and the week of pregnancy when the blood was drawn (R=-0,41). **Conclusions:** In pre-eclampsia the concentrations of PLGF were significantly lower and sENG were significantly higher when compared to normal pregnancy. It suggest the impaired process of the vascular formation in pre-eclamptic placenta. Moreover, the PLGF/sENG ratio was significantly higher in pre-eclampsia when compared to control group. The correlations between PLGF/sENG ratio and the indicators of disease severity were more profound when compared to correlations of single angiogenic factors and indicators of the disease. It suggest the potential usefulness of the PLGF/sENG ratio in the monitoring of the disease severity.

OP2-201

INCIDENCE OF CHROMOSOMAL ANEUPLOIDIES AT EMBRYONIC LEVEL WITH COMPARISON BASED ON MATERNAL AGE: FIRST RUSSIAN EXPERIENCE

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Introduction: Aneuploidy is the most frequent type of chromosomal abnormality in human oocytes resulting in early pregnancy loss, miscarriage, stillbirth, and developmental defects in fetuses and are common in preimplantation human embryos. Preimplantation genetic diagnosis for aneuploidy screening

(PGD-A) improve implantation and decrease miscarriage complications during the pregnancy. The present study is the first of its kind from Russia evaluating the incidence of aneuploidies along with the comparing based on maternal age used in IVF patients after performing PGD-A for 24-chromosomes. **Material & methods:** This is a retrospective cohort study of 1423 cycles including 4049 embryos (patients median age 34.7 ± 4.2 years, range 25–44) undergoing PGD-A for different indication including advanced maternal age, repetitive implantation failure, severe male factor infertility and recurrent miscarriage. Patients were divided in different age groups (25–30 years, 31–40 years, 41 years and more). The embryos were biopsied after IVF/ICSI, which include blastocyst stage embryos. The method involved whole genome amplification followed by arrayCGH (Agilent platform) technologies. Copy number variation analysis was accomplished using Cytogenomics software. **Results:** Of those 4049 embryos, 57,9% were euploid and 42,1% were aneuploid. Out of overall 1706 aneuploid embryos, 37,0% were complex aneuploid (with more than one aneuploidies), in 52,3% of cases we observed single aneuploidies, and 10,7% were disorders affecting part of chromosome. The fraction of single aneuploidy decreases and complex, multiple aneuploidies increase, affecting several chromosomes at once as the patient's age increases. Pic 1. The effect of patient age on the distribution of aneuploidy.



The involvement of different chromosomes in patients younger than 31 years and older than 40 years is different. For example, the involvement of chromosomes 16 and 22 is higher in older than 40 years than in women younger than 31 years, namely an increase in the trisomy of embryos with the mother's age for chromosome 16 and monosomy for chromosome 22. **Conclusions:** maternal age affects the number and composition of aneuploidy, affecting mainly different chromosomes in different age groups. This pilot study needs further detailed development. The reported study was funded by RFBR according to the research project #17-29-06041

OP2-202

FROZEN EMBRYO TRANSFER AFTER PGT-A CYCLES: WAIT OR NOT WAIT?

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Design: Retrospective cohort study that included 5104 cycles of FET of patients who underwent IVF-PGT-A at IVI centers between May 2016 and March 2017. **Materials and Methods:** A total of 913 FET cycles were included in the analysis. The preparation of the endometrium consisted of administration of oestradiol valerate (6mg/day) and micronized vaginal progesterone (400mg/12h). We compared FET cycle outcomes whether it was performed with the first menstruation after OPU (n=184) or delayed more than one month (n=700). We considered as primary outcome clinical pregnancy rate (CPR). Clinical results were analyzed using Student's t-test for means and chi-squared test for %. A multivariate logistic regression to quantify the effect of variables on PR was performed; the (OR) were expressed in 95% confidence intervals. Differences were considered to be significant if the probability of their occurrence by chance was 0.05. **Results:** There

were no statistical differences for age (38.7 ± 0.5 versus 38.6 ± 0.3 , $p = 0.780$), days of stimulation (12.7 ± 4.3 vs 11.6 ± 1.1 , $p=0.503$) and estradiol (2424 ± 366 vs 2383 ± 162 , $p=0.83$) or progesterone (0.7 ± 0.1 vs 0.8 ± 0.4 , $p=0.399$) levels the day of the triggering. Regarding clinical outcomes, similar results were obtained for both groups concerning MII s (11 ± 0.8 vs 10 ± 0.4 , $p = 0.03$), n°blastocysts (4.3 ± 0.4 vs 3.8 ± 0.2 , $p=0.122$), euploid embryos (2.1 ± 0.3 vs 1.8 ± 0.1 , $p = 0.039$) or TE (1.1 ± 0.1 vs 1.1 ± 0.2 , $p=0.52$). Finally, we did not find significant differences for clinical pregnancy rate (CPR) between groups (52.7% vs 54.9% , $p=0.33$). In multivariable logistic regression we found that the number of euploid (OR= 1.170, 1.062-1.288; $p=0.001$) and transferred (OR=2.530, 1.703-1.509; $p=0.001$) embryos significantly affected the probability of getting pregnant, while the timing of the FET (OR=1.090, 0.787-1.509; $p=0.604$) did not have a significant effect on this reproductive outcome. **Conclusions:** FET performed immediately after a freeze-all cycle showed equivalent results to delayed FETs in terms of pregnancy rates. In PGT-A cycles there is no need to wait: FET of euploid embryos can be performed in the subsequent cycle after OPU without compromising results.

OP2-203

A COST-EFFECTIVENESS EVALUATION COMPARING ORIGINATOR r-hFFH, BIOSIMILAR r-hFSH AND u-hFSH IN WOMEN UNDERGOING OVARIAN STIMULATION FOR ICSI

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Problem statement: We compared clinical effectiveness between the originator recombinant human follitropin alfa (O/r-hFSH), the biosimilar recombinant follitropin alfa (B/r-hFSH) and the FSH extracted from the urine of postmenopausal women (u-hFSH) in ovarian stimulation for ICSI. The aim of this study was to perform a cost-effectiveness analysis. **Methods:** 89 infertile women were enrolled. Exclusion criteria were: age 40, FSH (day 3-5 of the menstrual cycle) 30 mIU/ml, AMH 0.2 ng/ml. All participants received in the luteal phase, between days 15-21, a injection of triptorelin 3.75 mg. 18-20 days after, women were treated with a regimen of a daily dose of O/r-hFSH (22 patients, group A) or B/r-hFSH (27 patients, group B) or u-hFSH (40 patients, group C). Based on AMH and FSH levels, patients received FSH starting dose. When one or more follicles reached a diameter of 16 mm, 10,000 IU of hCG was given and 36 hours later, oocytes were retrieved. **Results:** No statistically significant differences were observed in the mean dose of FSH required. In 62% of total patients, there was a recovery of oocytes ≥ 4 and the best response was reported in group A (86% A vs 59% B vs 54% C): the median of the number of oocytes retrieved was statistically higher for group A ($p=0.003$). The 89% of women have retrieved at least one oocyte M2 and the median was 3 oocytes M2 (IQR 2-6); the median was 5 (IQR 4-8) for group A, 3 (IQR 1-6) for group B, and 2 (IQR 1-4) for group C ($p=0.006$). The clinical pregnancy rate per embryo transfer was 25% for group A, 45% for group B and 36% for group C. The cost per oocyte M2 was 148.88€ (O/r-hFSH), 221.20€ (B/r-hFSH), 161.91€ (u-hFSH), despite the cost of the O/r-hFSH for IU, in Italy, is higher than the others. **Conclusion:** The median of oocytes M2 retrieved was more relevant for O/r-hFSH. The clinical pregnancy rate was higher with B/r-hFSH, but in this group a higher percentage of blastocysts was transferred. The economic evaluation of this study, have shown a minor cost per oocyte M2 for O/r-hFSH.

OP2-204

DISTRIBUTION OF MTHFR ISOFORMS CARRIERS AND LEVEL OF HOMOCYSTEINE IN AN INFERTILE POPULATION WITH ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) CYCLE FAILURES

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Problem statement: Between 2016 and 2018 in 3 different clinics, male and female partners of couples suffering from long lasting infertility (2 years minimum) were screened for MTHFR (methylenetetrahydrofolate reductase) c677CT and c1298AC mutations. Homocysteine levels were measured and compared between wild type and mutation carriers. **Methods:** In total, 871 patients were included in the study and screened for c677CT; 294 patients were screened for both c677CT and c1298AC. 198 patients had a homocysteine controlled with a competitive immunoassay using direct, chemiluminescent technology. **Results:** 16.0% of the patients were wild type for both c677CT and c1298AC (84.0% of the patients were carrying at least one of the two mutations). 56.1% of patients (455/810) were carrying the c677CT mutation (43.5% in a heterozygous and 12.6% in a homozygous state); 50.6% of patients (149/294) were carrying the c1298AC mutation (40.4% in a heterozygous and 10.2% in a homozygous state). The average level of homocysteine among homozygous and heterozygous patients was significantly higher than among wild type patients (respectively 18.4 and 10.7 vs 7.9, $p=0.00005$ and $p=0.01$). **Conclusions:** MTHFR mutation incidence is high in the infertile population (84% of the patients carrying at least one of the two mutations). MTHFR mutations have an important clinical impact on fertility: implantation failures are fourfold higher in MTHFR c6777T homozygotes (Enciso, 2017) and sperm DNA defects are significantly higher in MTHFR mutations carriers (Cornet, 2017). The clinical impact of MTHFR can be due to the higher homocysteine levels in mutation carriers since MTHFR mutation decreases by up to 75% the capacity to generate 5MTHF. Treatments that support the one-carbon cycle allow a significant decrease in the homocysteine levels (Clement, 2018). Screening subfertile patients for MTHFR mutations (both c677CT and c1298AC) and treating the mutation carriers seems essential to improve their fertility and their ART outcomes.

OP2-205

INFLUENCE OF GENITAL INFECTIONS IN WOMEN WITH RECURRENT IMPLANTATION FAILURE ON IVF OUTCOMES

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Problem statement: Genital infections including mycoplasma, ureaplasma and chlamydia made harmful effects on reproductive health in both sexes. The prevalence of genital infections showed ethnic difference, and also the study in women with recurrent implantation failure (RIF) was scarce. The available evidence is inconsistent concerning the impact of female genital infection on the outcome of IVF. The aim of this study was to evaluate the prevalence of genital infections using multiplex PCR in women with RIF and evaluate the IVF outcomes regarding the genital infection. **Methods:** Case-control study was conducted in women with RIF. Mycoplasma hominis and genitalium, Ureaplasma urealyticum and parvum, Trichomonas vaginalis and Chlamydia trachomatis were tested using multiplex PCR by cervical swap before the initiation of IVF cycle. One hundred thirty six cycles were included. The harvested oocytes number, top quality embryo number, fertilization rate, implantation rate, clinical pregnancy rate, live birth rate and



miscarriage rate were analyzed depend on the genital infection. **Results:** Mean age of enrolled women was 35.20±4.79 years-old, mean parity was 0.13±0.45, and mean number of miscarriage was 0.81±1.49. Sexual transmitted infections were detected in 92 women (67.62%), *Ureaplasma parvum* was most common pathogen. *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Chlamydia trachomatis*, and mixed infections were followed. AMH level was 5.07±11.01 ng/mL, which was not different between two groups. Total doses of gonadotropin in each group were similar. Mean harvested oocytes in genital infection group were 8.12±5.48 compared with 9.09±6.56 in women without infection, which was statistically insignificant. Top quality embryos of each group were not different (2.53±1.59, 2.56±1.04, separately). Fertilization rates were also similar, however, implantation rate in women with genital infection was significantly lower than in women without infection. In women with genital infection, clinical pregnancy rate (16/92, 17.4%) and live birth rate (8/92, 8.7%) were also significantly lower than those of women without infection (31.8%, 22.7%). **Conclusion:** The female genital infections with mycoplasma/ureaplasma were prevalent in women with recurrent implantation failure. In women with those infections, implantation rate, clinical pregnancy rate, and live birth rate were significantly lower than women without infection. No disclosure of interest.

OP2-206

COMPARISON OF PREGNANCY OUTCOMES IN PATIENTS UNDERGOING INTRAUTERINE INSEMINATION (IUI) FOLLOWING OVULATION INDUCTION BY LETROZOLE VERSUS CLOMIPHENE CITRATE

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Problem Statement: Polycystic ovary syndrome (PCOS) causes chronic anovulation and is commonly associated with anovulatory infertility in reproductive age women (4 – 6%). Although clomiphene citrate (CC) is accepted as the first-line drug for ovulation induction in these women, response rate is low. Other options like costly GnRH injections and invasive laproscopic ovarian drilling are associated with ovarian hyperstimulation syndrome and multiple pregnancies. Aromatase inhibitors open a new chapter for ovulation induction in these patients. Hence, comparison of Clomiphene and letrozole is an interesting research prospect. **Methodology:** This randomised controlled study assessed 262 subjects with PCOS attending infertility clinic in department of OBG, TMMC between 2015 and 2018. Consenting women aged 18-39 years with BMI=35kg/m² with PCOS (Rotterdam criteria) and anovulatory infertility and at least one patent fallopian tube with partner's sperm concentration of at least 15 million/ml were included. Women with h/o ovarian surgery, diabetes or any severe medical illness, undergoing ART or male factor infertility were excluded. 106 subjects were recruited, allocated into 2 groups and administered Letrozole or Clomiphene from D2 to D6. Ovarian failure was considered if anovulation persisted. They were followed up with serial trans-vaginal ultrasonography. Injection HcG was administered 36 hours prior to planned IUI and check scan done for ovulation. The result was evaluated in terms of pregnancy outcome, endometrial thickness (D11-D14), ovulation rate, number of follicles, complications and failure. **Result:** Successful pregnancy outcomes were seen in 24 out of 52 with letrozole and 16 out of 54 subjects with Clomiphene. Mean endometrial thickness was 9-10mm with letrozole and 7.8-8.4mm with clomiphene. Ovulation occurred in 21 subjects with letrozole and 18 with clomiphene. A mean of 2-4 follicles developed with letrozole and 5-6 with clomiphene. Letrozole had lesser complications like multiple pregnancies. **Conclusion:** Successful pregnancy outcome was higher with letrozole despite less number of mature follicles. Letrozole could replace Clomiphene as the primary medication for chronic anovulation in PCOS. Furthermore, letrozole may be

advantageous in IUI, having lesser incidence of multiple pregnancies. It could augment or even obviate the use of gonadotropins for treatment of women with prior failure in achieving pregnancy with clomiphene citrate.

OP2-207

DIMINISHED OVARIAN RESERVE IN A NEWLY DIAGNOSED BREAST CANCER PATIENT WITH HETEROZYGOTE ATAXIA TELANGIECTASIA MUTATED (ATM) GENE MUTATION

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Problem statement: ATM is one of the genes that involves in double strand DNA break repair. Hereditary mutations of the ATM gene results in cancer susceptibility due to defective DNA repair mechanism. Double strand DNA break repair is also important in gametogenesis. It has been suggested that such defective mechanisms might associate with early follicular depletion. Herein, we report a diminished ovarian reserve (DOR) in a newly diagnosed breast cancer patient with heterozygote ATM gene mutation. **Methods: Case report.** Results: Patient: A 37 year old, recently diagnosed breast cancer patient was referred to our university IVF center to discuss her fertility preservation (FP) options before planned chemotherapy treatment. Her medical history included a gastric surgery due to stromal tumor 9 years ago. After surgery, she had been under close follow-up without need an adjuvant treatment. Due to a suspicion of genetic predisposition, genetic mutation screening was performed and result was matched with a heterozygote 549c ATM mutation. During follow up, biopsy was needed for a detection of 1.5 cm right breast mass and invasive ductal carcinoma was diagnosed. Mastectomy+SLNB was already planned as she come to our unit. Initial serum AMH, basal FSH, E2 tests and pelvic ultrasound was performed. The AMH result was 0.16 ng/ml, FSH, E2 level was 12.9 mIU/ml and 29 pg/ml, respectively. Detailed counseling was given about low ovarian reserve. After the surgery she applied for oocyte cryopreservation although given the low chance. Random start ovarian stimulation with rec FSH 300 IU plus letrozole 5 mg/day was started on luteal phase. On the sixth day of stimulation a left ovarian 18.5 mm follicle was observed and aspirated 36 hour after hCG trigger. Although repeated washing with aspiration, no oocyte could be obtained. **Conclusion:** Reproductive dysfunction has been reported in patients with Ataxia-Telangiectasia previously. Mutations in the ATM gene might be related with early follicular depletion. As far as we know this is the first report in the literature that demonstrates DOR in a patient with heterozygote ATM mutation. This mutation might associate with accelerated loss of ovarian reserve due to defective DSB repair in oocytes.

OP2-208

DOUBLE VITRIFICATION CYCLES YIELD HIGHER PREGNANCY RATES THAN FRESH CYCLES AND ONE-VITRIFICATION CYCLES

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Problem Statement: IVF techniques have been evolving for the last decades giving patients more chances to conceive healthy babies. However, only a few of them would increase the chances for difficult patients, mainly cancer patients and women over 40 years old. It is a common practice to preserve fertility by oocyte vitrification, or in case of poor responders, to make an oocyte



accumulation through different cycles. It also has been well reported the efficiency of frozen embryo transfer (FET) in a different cycle which significantly increases the pregnancy rate. The remaining challenge was for the patients that had a combination of both cases and would need to have their embryos re-vitrified. This problem has been decreasing since the introduction of a highly efficient vitrification method in 2012, which would keep survival even for the difficult patients. The aim of this work is to present the cases of double vitrification of oocytes-blastocysts in a retrospective study, reporting patients that underwent IVF cycles during 2017 and 2018. **Methods:** We compare the pregnancy rates of the cycles with double vitrification of oocytes-blastocysts vs. cycles of vitrified oocytes or blastocysts and the rates obtained from fresh cycles. We analyzed a total of 25 FETs of 19 patients (40 years old average). **Results:** The double vitrification cycles yielded to a higher pregnancy rate (84%; n=25), versus vitrified oocytes or blastocysts (47% and 48%; n=4,673 and n=15,177 in oocytes and blastocysts respectively) compared to fresh cycles (39%; n=115,610; SART, 2016). **Conclusions:** These results are an evidence of the safety and effectiveness of this improved method, keeping the precious life and quality of the embryos even after two vitrifications. With this high survival rate and excellent clinical results, ordinary methods are changing in to advanced fertility facilities all around the world.

OP2-209

KNOWLEDGE AND OPINIONS OF MIDWIFERY AND NURSING STUDENTS CONCERNING OOCYTE CRYOPRESERVATION

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Problem Statement: Social oocyte cryopreservation, which is the process of freezing oocytes with cryoprotectant and preserving them in liquid nitrogen at -196 °C to be used subsequently to delay pregnancy for social reasons, has attracted much attention recently. his study aims to observe students' thoughts on social oocyte cryopreservation and evaluate cultural outlook on oocyte cryopreservation in our changing society. **Methods:** The sample group consists of 342 female students who, between May and June 2018, were studying at midwifery and nursing departments of two private universities in Istanbul. Students who volunteered to participate in the research took an online or face-to-face survey prepared according to the relevant literature. The survey contained questions concerning the students' socio-demographic qualities, level of knowledge on oocyte cryopreservation and opinions on this topic. The data were analyzed using percentage and chi-square tests. Ethical permission was obtained prior to the study. **Results:** The participants consisting of midwifery (70.8%) and nursing (29.2%) students had an average age of 20.96±1.8 and most of them were single (98.2%). The question about the age at which women's fertility starts decreasing was answered as 37.64 on average. Students stated that they wanted to have children approximately at the age of 25. Of the participants, 59.1% reported having knowledge of cryopreservation and 38.2% stated having learned it from healthcare professionals. 45% said that they had never thought about freezing their own oocytes. 19.9% stated that they could use it to postpone having children for career reasons. 57.6% said that thanks to cryopreservation, women would be able to choose freely when they would be a mother. It is observed that the participants would consider oocyte cryopreservation mostly for medical reasons: cancer treatment affecting reproductive cells (63.7%), surgical intervention affecting the ovaries (59.9%) and risk of premature menopause (50.3%). **Conclusion:** It was found that midwifery and nursing students at two private universities in Istanbul had a positive attitude towards oocyte cryopreservation, although they would consider it if required

for medical reasons. No significant difference was found in their level of knowledge. The authors do not have any conflicts of interest to declare.

OP2-301

DISTRIBUTION OF MTHFR ISOFORMS CARRIERS AND LEVEL OF HOMOCYSTEINE IN AN INFERTILE POPULATION WITH ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) CYCLES FAILURES

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Problem statement: MTHFR (Methylenetetrahydrofolate reductase) isoforms induce defective folic metabolism and affect the recycling of homocysteine to methionine. The increased levels of homocysteine due to MTHFR polymorphisms is responsible of oxidative stress (Guo, 2016). Oxidative stress is a common cause of infertility and ART failures. MTHFR isoforms are responsible of spermatozoa anomalies, especially via a defect in nucleus compaction (Cornet, 2017). Furthermore, the IVF embryos originating from MTHFR isoforms carriers have high chromosomal problems for the heterozygotes and higher in the homozygotes patients (Enciso, 2017). **Methods:** From January 2016 to January 2018, we followed 198 women patients suffering from infertility and having had at least 2 ART (Assisted Reproductive Technologies) cycles failures. All those patients were tested for MTHFR isoforms and we also measured their level of circulating homocysteine. We compared those results among our infertile population and with the general population. **Results:** Among the infertile population of our study, 63.6% of the patients are carrying the MTHFR mutation (43.9% in a heterozygous and 19.7% in a homozygous state). This proportion is significantly more important (p<0.05) than the proportion of patients carrying MTHFR mutations in the general population: 50.5% (Zappacosta, 2009). The average level of homocysteine in homozygotes and heterozygotes patients is significantly higher than the average level of homocysteine in wild type patients (respectively 10.7 and 8.8 vs 7.9, p=0.01 and p=0.02). In total, the average level of homocysteine in MTHFR carriers (homozygotes+heterozygotes) is significantly higher than the average level of homocysteine in non carriers (wild type) patients (9.4 vs 7.87, p=0.02). **Conclusion:** Infertile patients with ART cycle failures should be tested for MTHFR mutations and their homocysteine levels should be measured. Indeed, the affected patients could benefit from a treatment available allowing to bypass the problems linked to MTHFR impaired activity and thus decreasing oxidative stress, and improving their ART outcomes.

OP2-302

PREIMPLANTATION GENETIC SCREENING IN PATIENTS WITH RECURRENT PREGNANCY LOSS

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Problem statement. Recurrent pregnancy loss (RPL) is defined as 2 or more spontaneous pregnancy losses up to 20 - 22 weeks of gestation. IVF with preimplantation genetic screening (PGS) for aneuploidy has been proposed as a treatment option for women with RPL. The aim of the study was to analyze the effectiveness of PGS in the IVF cycles in patients with RPL and infertility. **Methods.** The study included 196 patients with normal karyotype and RPL history. The patients were stratified into 2 groups: group 1 (n=96) - women with IVF+PGS, and group 2 (n=100) - women with IVF. Blastocyst biopsy was analyzed by aCGH. All embryos underwent



vitrification in both groups. **Results.** The clinical pregnancy (CPR) and live birth (LBR) rates were higher in the PGS group (45.8% vs 29.0%, $p=0.0148$ for CPR, 35.4% vs 17.0%, $p=0.0033$ for LBR). We performed stratification analyses to study the effectiveness of PGS depending on the maternal age. The age of the women in the study was 23 to 47 years (mean age (35.7 ± 5.3) years, and generally had no effect on CPR or LBR. After the exclusion of older patients from the analysis, the lowest odds and area under curve (AUC, c-statistics) were in women of 23-29 years old that make the age of 30 to be the lower threshold value. After the exclusion of younger patients from the analysis, the lowest odds and AUC were in women of 40-47 years old that makes the age of 39 to be the higher threshold value. Thus, PGS by aCGH increased the odds for the live birth in patients with RPL at the age of 30 to 39 years, and did not increase it in the patients of 29 years and younger and in the patients of 40 years and older. **Conclusion.** Aneuploidy screening by aCGH resulted in statistically significantly improved IVF outcomes in patients with RPL. CPR was 1.6-fold higher and LBR was 2.4-fold higher in the subgroup of patients of middle maternal age 30-39 years. The authors report no conflicts of interest.

OP2-303

THE IMPACT OF PTEN INHIBITION AND LOW DOSE RAPAMYCIN ON PRIMORDIAL FOLLICLES ACTIVATION AND DNA DAMAGE RESPONSE OF BOVINE OVARIAN FOLLICLES IN VITRO

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Problem statement: Regulation of primordial follicle activation has major clinical implications but it remains poorly understood. Inhibition of Phosphatase and tensin homolog (PTEN) is known to activate primordial follicles but may compromise further developmental potential, with oocytes showing increased DNA damage and reduced repair capacity. The mammalian target of rapamycin (mTOR) signaling pathway is a master regulator of cell growth and metabolism and its inhibition attenuates follicle growth activation. We hypothesised that combined *in vitro* inhibition of both PTEN and mTOR would increase follicle activation without compromising oocyte DNA damage and repair capacity. **Methods:** Bovine ovarian fragments sized 4x2x1mm were exposed to medium containing 1) 1 μ M of bpv(HOPic), a PTEN inhibitor, 2) 0.1nM rapamycin (mTOR inhibitor), 3) 1 μ M bpv(HOPic)+0.1nM rapamycin, or 4) control medium for 24 hours. Tissue was incubated for a further 5 days in control medium then fixed and analysed histologically by immunohistochemistry using antibodies against γ H2AX, a marker of DNA damage, and the DNA repair proteins MRE11, ATM and Rad51. **Results:** Tissue exposed to either 1 μ M bpv(HOPic) or 1 μ M bpv(HOPic)+0.1nM rapamycin contained a significantly higher proportion of growing follicles (81.9% and 70.2% respectively) compared to control (50.9%) and 0.1nM rapamycin (50.2%) ($p \leq 0.001$ for all groups) (12,242 follicles analysed). Expression of γ H2AX in oocytes in primary follicles was highest in 1 μ M bpv(HOPic) (64.5%) compared to control (44.4%), 0.1nM rapamycin (33.7%) and 1 μ M bpv(HOPic)+0.1nM rapamycin (29.5%) ($p \leq 0.05$ for all groups). Expression of MRE11, ATM and Rad51 was reduced in oocytes of primary follicles exposed to bpv(HOPic) (69.5%, 30.1% and 31.3% respectively) compared to control (97.5%, 65% and 90.6%) ($p \leq 0.05$ for all groups), whereas in oocytes exposed to 1 μ M bpv(HOPic)+0.1nM rapamycin, expression of MRE11 (85.7%) and ATM (65.3%) were similar to control ($p > 0.05$ for all groups) but Rad51 which was significantly lower ($p = 0.001$). **Conclusion:** Exposure of bovine follicles to bpv(HOPic) for 24 hours resulted in increased primordial follicle

activation, but with increased DNA damage and reduced DNA repair capacity in oocytes. The addition of a low dose rapamycin to bpv(HOPic) reduced DNA damage and improved DNA repair capacity of the oocytes whilst maintaining follicle activation. This may be a promising strategy for the derivation of mature oocytes *in vitro*.

OP2-304

LIPID DISREGULATION IN SEMINAL AND FOLLICULAR FLUIDS COULD AFFECT GONADAL RESPONSE

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Problem statement: There is evidence that supports the role of lipids in male and female infertility. Lipids are involved in basic molecular processes for reproduction, although little is known about their impact on male and female gametes. Our group has recently showed associations between seminal plasma and follicular fluid concentrations of lipids with altered sperm parameters and low ovarian reserve, but it is also important to consider the confounding factor of age and body mass index (BMI), both related to the lipid profile and fertility. Our objective is to obtain, through principal component analysis (PCA), a lipid profile in plasma common for men and women, and also specific lipid profiles in seminal plasma and follicular fluid to evaluate quantitatively, the effect of lipid metabolism on the gonadal response regardless of age and BMI. **Methods:** In this prospective study, 41 follicular fluid and serum samples of IVF-ICSI cycles and 42 seminal plasma and serum samples of males in the infertility study were analysed for cholesterol, triglycerides and non-esterified fatty acids using a DAOS method and colorimetric enzymatic method. The parameters used to assess gonadal response were number of motile spermatozoa and number of oocytes in metaphase II. Differences between groups were studied by means Principal Component Analysis, Kolmogorov-Smirnov test, Pearson correlation, Student's T and multivariate linear regression. **Results:** Using a multivariate linear regression model to exclude the effect of the age and BMI, we found that the lipid profile in follicular fluid and plasma influence inversely, significantly and independently of age on ovarian response and the number of matured oocytes recovered. Moreover, we found that both age and seminal lipid levels are predictors of seminal quality independent of each other and independent of plasma lipid values. Plasma lipid profile is not related to seminal quality according to the rest of variables. **Conclusion:** Our current analysis further reinforces the association of both low ovarian response and low number of motile sperm with abnormal lipids levels. Our findings are the first to demonstrate that lipids in follicular and seminal fluid are associated with reduced gonadal response as measured by an ACP method.

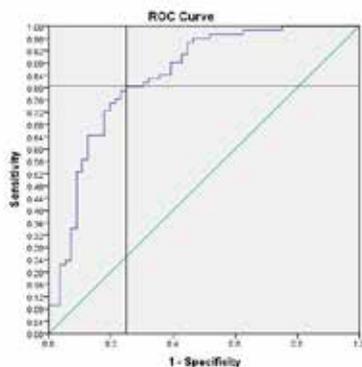
OP2-305

ENDOMETRIAL AND MYOMETRIAL VASCULARITY AS PREDICTORS OF IMPLANTATION OUTCOME

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Problem statement: To investigate the effect of endometrial and myometrial vascularity on IVF (In-Vitro Fertilization) pregnancy rate using Vaginal power Doppler ultrasound. **Methods:** This is a prospective study on 168 IVF cycles performed at AL HADI IVF center. For each patient, in addition to her age and day of transfer, the following ultrasonographic and power doppler parameters were recorded on the day of transfer: distance between transferred embryos and the fundus, endometrial thickness, endometrial VI (Vascular Index), endometrial VFI (Vascular Flow Index), myometrial VI and myometrial VFI. Biochemical and ultrasonographic pregnancy were checked 2 weeks and 3 weeks after embryo transfer, respectively. Using all these variables, a model was formulated using logistic regression and a Receiver operating characteristic (ROC) curve analysis showing the performance of our model on predicting implantation outcome was done. **Results:** The biochemical and ultrasonographic evidenced pregnancy rates were higher among patients with lower endometrial and myometrial vascular index and vascular flow index. The algorithm developed was able to accurately predict pregnancy with a sensitivity of 84.2% and a specificity of 62.5%. The area under the ROC curve was 0.837, indicating a good predictive value of this new model to predict pregnancy outcome in IVF patients. **Conclusion:** The endometrial and myometrial vascularity have significant effect on implantation rate in IVF. It is the first paper to find such a correlation. Disclosure of interest: None declared



OP2-306

GENETIC SCREENING RESULTS OF WOMEN WHO UNDERWENT IVF TREATMENT ACCORDING TO THEIR IVF INDICATION: SINGLE CENTER EXPERIENCE

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Objective: Our aim in this study is to assess the genetic screening outcomes and cost-effectiveness in infertile couples who underwent IVF treatment due to male factor, poor over response

and IVF failure. **Materials-Methods:** A total of 884 patients (375 female, 509 male) were included and divided as male factor (n=313), poor ovarian response (n=95) and IVF failure (n=627) and underwent genetic screening between January 2011 and December 2015 at a tertiary center. 323 fertile couples (323 female and 323 male) with at least one spontaneous clinical pregnancy history and genetic screening in our hospital were identified as the control group. IVF failure group is defined as two or more unsuccessful IVF trials in the patient's history. Poor ovarian response is defined according to ESHRE Bologna criteria. Patients whose total motile sperm count was determined below 5.10^6 had genetic counseling for male factor. All data were recorded retrospectively. 'Number needed to treat' value for the determination of an abnormal chromosomal structure was calculated. **Results:** Mean age of the participants was 32.16 ± 4.94 . The presence of abnormal karyotype was more common in the study group (5.9%; 52/884 vs. 2.8%; 18/646) ($p=0.003$). People need to be scanned for the determination of an abnormal karyotype was calculated as 31. Additionally, abnormal karyotype was detected more frequently in male factor subgroup (9.6%; 30/313 vs. 3.1%; 10/323) ($p=0.001$). Number of infertile men needed to be scanned for the determination of an abnormal karyotype was calculated as 15. On the other hand, the frequency of abnormal karyotype was statistically similar between control group and poor over response group ($p=0.068$) or IVF failure group ($p=0.103$). **Conclusion:** Infertile population has higher abnormal karyotype than fertile population. Patients who undergo ART because of the male factor have a higher risk of abnormal karyotype, but this risk is lower for the patients with poor over response and history of IVF failure. Our findings are consistent with the literature. Routine genetic screening in IVF patients with poor over response and history of IVF failure appears to be costlier than that due to male factor. For this reason, novel studies are needed in selected patient groups.

OP2-307

INVESTIGATION OF THE ROLE OF SERUM TELOMERASE LEVELS IN PATIENTS WITH OCCULT PRIMARY OVARIAN INSUFFICIENCY

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Problem Statement: Occult primary ovarian insufficiency (POI), is an early stage of POI which is defined as infertility, elevated day 2-3 follicle stimulating hormone (FSH) levels and presence of regular menstrual cycles. This study was designed to investigate serum telomerase levels of patients with occult POI and the relationship between in vitro fertilization (IVF) results of these patients and serum telomerase levels. **Methods:** This cross sectional case control study was conducted between May and October 2017, including 78 patients at Zekai Tahir Burak Hospital Reproductive Endocrinology Department. Occult POI was defined as women 40 years age with a history of FSH elevation between 12IU/L- 25IU/L and low ovarian reserve before initiation of IVF (n=39). Controls were patients attending the hospital for contraception, with no history of infertility, having at least one healthy child (n=39). The groups were matched for age and body mass index (BMI). All patients and controls were monitored for basal hormone levels and assessed for antral follicle counts (AFC) on days 2 and 3 of the menstruation. Additionally, anti-mullerian hormone (AMH) levels, controlled ovarian hyperstimulation protocol, induction parameters and clinical pregnancy results of occult POI patients were recorded. Enzyme-Linked ImmunoSorbent Assay method was used to determine telomerase levels in serum samples. **Results:** The mean age and BMI of the patients and controls were $32(29-35,5)$ years versus $31(28-35)$ years, $24.53 \pm 4.10 \text{ kg/m}^2$ versus $25.58 \pm 4.08 \text{ kg/m}^2$,



respectively. There were no statistically significant differences in serum estradiol, prolactin, thyroid stimulating hormone levels between the groups. There were no statistically significant differences in serum telomerase levels in patients (3,83±0,80 ng/mL) when compared with the control group (3,73±0,81 ng/mL) (p=0,589). There was no statistically significant correlation between serum telomerase levels and AMH levels, parameters of induction, oocyte and embryo numbers of occult POI group. **Conclusion:** This is the first study in the literature investigating serum telomerase levels of occult POI patients according to our knowledge. There is no statistically significant difference in serum telomerase concentration between the groups. Further studies with larger populations will shed light on the literature. **Keywords:** occult primary ovarian insufficiency, telomerase, in vitro fertilization, reproductive aging

OP2-308

IMPROVED VITRIFICATION METHOD YIELDS TO THE HIGHEST WORLDWIDE POSITIVE PREGNANCY OUTCOMES COMPARED TO FRESH CYCLES

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Problem Statement: Many techniques for preservation of oocytes and embryos have been developed during the past 2 decades due to the increasing demand of fertility preservation, either because of health conditions or maternity delay. For this reason, vast clinical results exceed 2,000,000 cases in over 73 countries, in which the open system of vitrification has been able to make 90% of human oocytes and embryos survive after freezing. Despite the variety of techniques, many of them require very skilled manipulation and complicated protocol; besides, none of them had reached a high survival rate that would consider the fragility of the oocytes of cancer patients or women over 40 years old. A remaining challenge was to rescue valuable oocytes and embryos that still had led to death by creating an improved noninvasive vitrification method that gives possibilities to women in true difficulty and pain. The aim of this work is to present the world-wide results of a very successful vitrification method for oocytes and blastocysts. In this retrospective study we report patients undergoing IVF cycles during 2015-2017 with either oocyte or blastocyst vitrification in clinics worldwide. **Methods:** We show the hidden improvements of the vitrification method in order to obtain the best survival rates for oocytes and blastocysts. We also compare the pregnancy rates of the cycles with vitrified oocytes and blastocysts with the rates obtained from fresh cycles. **Results:** The modifications featured in this new technique yield to a worldwide higher pregnancy rate (47% and 48%; n=4,673 and n=15,177 in oocytes and blastocysts respectively) compared to fresh cycles (39%; n=115,610; SART, 2016). **Conclusions:** These results are an evidence of the safety and effectiveness of this improved method. With this high survival rate and excellent clinical results, ordinary methods are changing in to advanced fertility facilities all around the world.

OP2-309

ISOLETED TERATOZOOSPERMIA DOESN'T NEGATIVELY IMPACT FERTILIZATION, EMBRYO DEVELOPMENT AND IMPLANTATION RATES WHEN USING INTRACYTOPLASMIC SPERM INJECTION (ICSI) VS IN VITRO FERTILIZATION (IVF) AS AN INSEMINATION METHOD.

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Problem Statement: Zhu Y. et al 2013, compared the fertilization rate in patients with teratozoospermia versus couples with a normal morphological parameter in semen sample; when ICSI was used to treat these teratozoospermic couples, improvement in fertilization was observed. However, the quality of embryos, the blastocyst formation rate, and the pregnancy rate of these couples were not better with ICSI. On the other hand, Keegan B. et al 2013, observed that teratozoospermia generally does not impact on the outcome of in vitro fertilization treatment, these patients do not necessarily need to be subjected to a more invasive insemination method such as ICSI. **Material and methods:** A total of 197 IVF cycles from women under 35 years old between January 2017 and May 2018 were analyzed. The inclusion criteria for this retrospective study were couples with a male factor whose diagnosis was specifically isolated teratozoospermia. Of the total oocytes recovered by cycle per patient, half of them were inseminated by ICSI and the other half by conventional in vitro fertilization. The correct fertilization rate was evaluated for each insemination method, number of good quality embryos on day 3 and 5 of development, implantation rate, gestation and abortion was calculated too. **Results:** No significant difference was found between the two groups. The fertilization rate was 86% by ICSI method vs 82% by conventional IVF, number of good quality embryos on day 3 was 42% vs 45% respectively, number of good quality embryos on day 5 was 33% vs 39% respectively, implantation rate was 47% vs 43% respectively, gestation rate 61% vs 62% respectively and abortion rate 4% vs 5%. **Conclusions:** According with the analysis of the results, we did not observe statistically significant differences in the parameters analyzed when comparing the inseminated method of patients with isolated teratozoospermia, good fertilization, embryo development, gestational and implantation rates in both cases were observed. Therefore, the use of one or another technique for oocyte insemination in this group of patients is recommendable.

OP2-401

MATERNAL OBESITY AND RECTOVAGINAL GROUP B STREPTOCOCCUS COLONIZATION AT TERM

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Introduction: Maternal obesity has been proposed as risk factor for GBS colonization. The biological mechanism that explains the relationship is uncertain, but some studies showed the change of the intestinal microbiome in obese women as a possible cause. **Objective:** To test the hypothesis that maternal obesity is an independent risk factor for GBS colonization. **Study Design:** Retrospective cohort study of women with low risk pregnancies admitted in labor at ULSAM during three years. This is a case-control study comparing maternal BMI between women with positive GBS colonization and a control group of women who had negative culture. The statistical significance evaluated by the Chi-square and Student's t-test, *p* **Results:** A total of 2534 women were involved in this study, 489 (17,1%) pregnant were a positive GBS colonization and 11.2% of women have obesity. In terms of BMI, group with pregnant women with GBS colonization has a higher BMI pre-pregnancy than pregnant women without colonization, but there are no significant differences (p=0,38). Additionally obese women (13,7%) were not significantly more likely to be colonized by GBS when compared with no obese women (12,3%), (p=0,52). These results may be explained by the low prevalence of colonization in this sample, which is lower than that reported in the literature, and because the sample is only composed by white women. The high rate of false negative GBS culture described in the literature may explain these results. **Conclusion:** In this study, maternal obesity doesn't appear to be



a predictor of GBS colonization, however more studies are needed.

OP2-402

IS THE IADPSG SCREENING FOR GESTATIONAL DIABETES BETTER THAN THE TWO-STEP STRATEGY IN THE DETECTION OF DIABETES OR GLUCOSE INTOLERANCE IN POSTPARTUM?

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Problem statement: Introduction of IADPSG (International Association of Diabetes in Pregnancy Study Group) criteria for the screening of Gestational Diabetes Mellitus (GDM) has led to a higher prevalence of GDM without any certainty about short or long-term advantages. We conducted an observational study whose primary objective was to assess if one-step IADPSG criteria for GDM screening (universal 75 Oral Glucose Tolerance Test - OGTT) has a better sensitivity for the detection of glycaemic anomalies (Type 2 diabetes -T2DM- impaired fasting glucose or glucose intolerance) in the post-partum (PP) period than the two-step criteria as recommended by the American Diabetes Association (ADA) in 2003 (50g Glucose Challenge Test -GCT- followed by a 75g OGTT if GCT is positive). **Methods:** Recruited patients were given a 50g GCT at 24 to 26 Weeks Gestation (WG) and a 2h 75g OGTT between 26 and 28 WG. Results of the 50g GCT were blinded to both patients and carers. GDM screening was done with IADPSG criteria. Three months PP we prescribed, to all GDM subjects and a subgroup of normoglycemic subjects who agreed to further testing, a screening for glycaemic anomalies with a 2 hours 75g OGTT. Unblinding the result of the 50g GCT, and re-interpreting of OGTT according to ADA thresholds, allowed comparison between the two strategies. We calculated the sensitivity of each strategy to detect glycaemic anomalies in PP. We used a Mc Nemar's chi2 test to assess statistical significance. Alpha was set at 0.05. **Results:** 1006 patients were enrolled at first trimester and 109 patients completed the study until PP screening. Of these patients 10 were diagnosed with glycemic anomalies in PP. The IADPSG criteria allowed for the detection of 7/10 glycemic anomalies, sensitivity 70%, 95%CI 34.75-93.33. The two step criteria detected 2/10, sensitivity 20% 95%CI 2.52-55.61. The p-value of the McNemar chi2 test was 0.02 **Conclusions:** Although our study is flawed by a high rate of lost to follow up in the PP period, the data shows that IADPSG criteria have a higher sensitivity than the two-step criteria for detecting glycemic anomalies in the PP period.

OP2-403

HYPNOSIS IN CHILDBIRTH

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Childbirth is often the most memorable event in a woman's life. A heightened state of awareness is almost always inevitable. During this state of heightened awareness, in presence of physical and emotional stress and often great physical discomfort, the patient is extremely open to hypnotic suggestion. Presented are some useful hypnotic tools for recognizing needs and treating patients during labor and delivery. Two cases of formal hypnosis are presented: The first is a case of a post trauma patient whose trauma was from a catastrophic car accident ten years prior to her pregnancy. During the first moments after the accident she was treated in the usual way in the acute trauma emergency room in a hospital, but her recollection of the incident was of group rape. She had an elective

Cesarean delivery with hypnosis and regional anesthesia. The second case is an officer in the Israeli Defense Force in her third delivery having only hypnosis for pain control. Included is a full recording of the pre-labor session and of the actual birth. In conclusion some practical hypnotic techniques are presented for use in appropriate cases.

OP2-404

FETOMATERNAL MEDICINE DEPARTMENT ADMISSIONS IN A TERTIARY CARE HOSPITAL

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Problem statement: Fetal and maternal complications may be serious enough to motivate hospital admission and justify a preterm delivery (either spontaneous or iatrogenic), fetal and/or maternal death. Preterm delivery remains the main cause of child morbimortality worldwide, namely in developing countries. Nevertheless, World Health Organization data indicates that preterm birth rates are increasing. Besides, as maternal age increases, complications related to previous health conditions are more frequent. Hypertension and preeclampsia are a major concern and precocious diagnose and treatment are vital to avoid fetal and maternal problems. We aimed to assess the reasons for admission in our tertiary fetomaternal medicine department and following pregnancy outcome to understand the main problems in our daily practice and perform a better care. **Methods:** Review of all admissions in our fetomaternal medicine department between July and December 2017, namely admission reason, maternal age, gestational age at admission and at delivery and type of delivery. Data were analyzed using IBM SPSS Statistics 21. **Results:** During this 6-month period, 317 admissions were registered, referring to 298 pregnant women (19 patients were readmitted) including 26 twin pregnancies. The most frequent admission reason was threatened preterm delivery (91 admissions, 28%), followed by preeclampsia (40 admissions, 13%), fetal growth restriction (34 admissions, 11%), fetal anomalies (27 admissions, 9%) and preterm premature rupture of membranes (20 admissions, 6%). Other causes of admission included bleeding, oligohydramnios, intrahepatic cholestasis of pregnancy or intrauterine fetal demise. Mean gestational age at admission was 30 weeks, being the minimum 6 weeks in a patient admitted for retained products of conception. 29 patients had delivery in another facility. Among those who delivered in our hospital, and reached the limit of viability, (123) 46% delivered before 37 weeks, 7 of them at or with less than 28 weeks. Caesarean section (CS) represented 51% of deliveries, which is superior to the percentage of CS in our hospital in 2017 (27%). **Conclusion:** Threatened preterm delivery was the main motive of admission followed by preeclampsia. Almost half of patients who had reached fetal viability had a preterm delivery raising concerns about how to improve fetomaternal medicine practice in this area.

OP2-405

POSTPARTUM MYSTERY- TUBERCULOSIS

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The peritoneum is the most common site of extrapulmonary tuberculosis; however presentation in the postpartum period is extremely rare, Diagnosis of abdominal TB is often difficult due to its nonspecific, clinical, laboratory and radiological findings. **Materials:** We report 2 cases, One A 30-year-old P1L1 delivered by normal vaginal delivery, presented to us on postnatal day 15 with complaints of fever and abdominal pain, hemoglobin of 8.8,



Total count of 11,800 with elevated polymorphs urine and vaginal culture both positive for E.Coli. She was treated as a case of PID, with higher antibiotics. On acute exacerbation of symptoms, the patient was shifted to ICU care. CT abdomen and ascitic fluid tap were done, which showed features suggestive of peritonitis, ADA and LDH were deranged Hence patient underwent a diagnostic laparoscopy. Our second case was a 30-year-old P2L2 previous 2 LSCS, who presented with abdominal pain 1 month postpartum and had been regular treatment at an outside hospital for chronic pelvic pain. her symptoms continued for 10 months with vague abdominal pain, irregular menstrual cycles, elevated CA 125 and Ultrasound abdomen showed free fluid in the abdomen in the parietal wall, A mass was palpable in the right iliac fossa accompanied with tenderness and she was taken up for diagnostic laparoscopy. **Results:** Case 1 showed Extensive peritonitis, adhesions from omentum and bowel to the anterior abdominal wall. Uterus adherent to the urinary bladder and anterior abdominal wall, frank pus seen. An omental biopsy taken showed granulomatous inflammation consistent with tuberculosis. Postoperatively she was started on Antitubercular treatment. Case 2 which revealed multiple tubercles, a tuboovarian abscess, inguinal mass with dense caseous material and peritoneal biopsy showing granulomatous lesion consistent with tuberculosis. Ascitic fluid showed elevated LDH (9000) and ATT was started. **Conclusion:** Tuberculosis may mimic many diseases such as UTI, Ovarian malignancies. A flare-up of TB leads to Tb peritonitis in the postpartum period, although rare clinical suspicion of the same will help in early diagnosis and prevent the complications that follow.

OP2-406

DETERMINING THE SELF-CARE AGENCY AND THE HEALTH PRACTICE LEVELS OF THE PREGNANT WOMEN AND THE EFFECTIVE FACTORS

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Problem statement: The purpose of this study is to determine the self-care agency levels and health practices of pregnant women and the effective factors and to examine the correlation between the self-care agency and the health practices. **Methods:** This study was conducted in descriptive and correlational design. The sample of this study consisted of 530 pregnant women who were living in the city center of Malatya, were having different cultural characteristics and applied to 3 different Family Health Center. The pregnant women, who agreed to participate in the study, were included in the study with the improbable random sampling method. The data were collected between October 2017 and May 2018. "Questionnaire", "The Health Practices in Pregnancy Scale", and "Self-Care Agency Scale" were used to collect the data. **Results:** A statistically positive significant correlation was determined between the self-care agency scale total mean score and the health practices scale total mean score of the pregnant women ($r:0.766$, $p=0.000$). It was found that the difference between the Self-Care Agency Scale and Health Practices Scale total mean scores was statistically significant according to the ages, educational levels, and employment status of pregnant women, educational level of their husbands, the occupation of their husbands, their residence places, their financial situation, their family types, parity, number of their living children, the number of having prenatal care and whether they intended pregnancy or not ($p0.001$). According to the gestational weeks, it was found that only the difference between the total mean scores of the Self Care Agency Scale was statistically significant ($p 0.001$). **Conclusion:** It was found that the self-care agency levels and health practices of the pregnant women were at medium-level and their health practices increased as their self-care agency levels increased. **Key words:** pregnancy period, self-care agency, health practice,

midwife, nurse.

OP2-407

SUCCESSFUL NON-SURGICAL MANAGEMENT OF SECOND TRIMESTER HETEROTROPHIC ABDOMINAL PREGNANCY

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Problem statement: Heterotopic pregnancy is an increasingly common complication of assisted reproductive technique. Abdominal pregnancy is a rare and life threatening form of ectopic pregnancy that can present as an extra uterine portion of heterotrophic pregnancy. Objective of study was How to get good outcome of intrauterine pregnancy with minimal invasive approach. **Method:** Study was conducted during 2007 to 2017 at Life Medicare Hospital, Faisalabad. Total ten cases of heterotrophic pregnancy were reported, four were included due to second trimester and hemodynamical stability. Both extra uterine and intrauterine foetus were alive and intra uterine foetal anomaly were ruled out. All basic investigations and clotting profile were done. After counselling and taking consent from the patient, abdominal foetuses were made dead by KCL (Potassium Chloride) injection under ultrasound guidance. Patient were kept under observation for 3-4 days and then discharged. **Results:** Post procedure, pain gradually settled down, peritoneal fluid started decreasing. Intra-uterine foetuses grow on normal parameters, except one foetus which developed intra-uterine growth retardation due to hypertensive mother. Mode of delivery was c-section and delivered between 36 to 38 weeks. The extra uterine foetuses were removed from the abdomen without any complication. No extra transfusion was given to the patients. Follow-up beta ECG showed normal decline. No methotrexate needed postoperatively. **Conclusion:** Mortality and morbidity of mother and intra uterine foetus can be reduced by making the abdominal foetus dead. If we allow to grow the abdominal foetus, it can create life threatening conditions for mother with higher rate of mortality and morbidity. The abdominal foetus has higher chance of congenital anomalies due to location and higher rate of mortality and morbidity due to pre-maturity. Further studies are required to make this approach as a definite plan of management. Either this method will be helpful if the pregnancy is more advanced? whether the clotting profile will be disturbed by making one foetus dead in more advance stage of pregnancy is an area for further research. Application of this method for hemodynamically unstable patient by giving blood transfusion and making the abdominal foetus dead is also an area of concern.

OP2-408

THE EFFECTS AND RELATED FACTORS OF HEALTH LITERACY STATUS AND SELF-EFFICACY OF PREGNANT WOMEN

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Problem statement: Self-efficacy is the belief in the ability to demonstrate effective behavior regarding events that affect an individual's life. Self-efficacy influences patients', health/illness status, exchange of information, information recall and use of it, use of health care, the satisfaction level of service, and self-management and its outcome. **Methods:** The aim of this descriptive study was to determine the factors related to self-sufficiency and health literacy level of pregnant women. The study was conducted at a maternity hospital in the Central Anatolia region of Turkey. 175 people were calculated with the G * Power 3.1.7 program in the sample. 205 pregnant women were included to

prevent data loss. The data was collected in a descriptive form containing socio-demographic and obstetric characteristics and general self-efficacy and health literacy levels. Descriptive statistics, correlation, student t-test, chi-square, variance and regression analysis were carried out. **Results:** A total of 205 pregnant women with a mean age of 26.66±6.30 years participated. The average self-efficacy score of the pregnant women was determined as 32.92 ± 7.131 (min = 15, max = 50) and their general health literacy index score average as 58.00 ± 8.15 (min = 42, max = 83). 11.7% of pregnant women had inadequate, 44.4% had problematic-limited, 29.8% had adequate and 14.1% had excellent health literacy. It was found that those with high health literacy received preconception counseling, had regular health checks and used folic acid, and were physically active more than three days a week. It has been determined that pregnant women with a high self-efficacy level received preconception counseling, had health checks, began using iron preparations, had blood tests and were physically active throughout their pregnancy. It was determined that there was a correlation between health literacy and self-efficacy score averages of pregnant women at $p = 0.000$ significance level. **Conclusion:** Health literacy of pregnant women was determined at a moderate level. Individuals with higher levels of health literacy and self-efficacy displayed positive behavior in the preconception period. Self-efficacy was found to be an important factor in explaining the level of health literacy.

OP2-409

DO PATIENTS TAKE RESPONSIBILITY FOR THEIR OWN SAFETY? A QUESTIONNAIRE-BASED SURVEY IN A MULTI-ETHNIC NORTH LONDON POPULATION

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Problem Statement: An estimated 850,000 cases of unintentional medical injuries occur every year, at least half of which are thought to be preventable. Obstetrics and Gynaecology is a specialty with high medical malpractice costs, some of which can be attributed to medical errors. Active patient participation in their own safety has well-demonstrated benefits in reducing errors, especially in relation to hand-washing and surgical site marking, and several strategies to increase patient participation have been employed in recent years. Understanding how patients feel about participating in their own safety and how to improve engagement in safety behaviours could help to reduce medical errors in Obstetrics and Gynaecology. The authors sought to examine patient participation in a range of safety-related behaviours and investigate how they varied with different patient demographics. **Methods:** A 20-point questionnaire examining safety-related behaviours was given to surgical and gynaecological patients at a multi-ethnic North London teaching hospital. The questionnaire explored patient willingness to question healthcare professionals about their treatments and medications, challenge staff on infection control procedures and participate in accurate history-taking. Data on sex, age, ethnicity, English language proficiency, duration in the United Kingdom, employment and education status was also collected. **Results:** 195 patients were invited to participate in this study and 175 patients completed the questionnaires. Female patients who had tertiary education, those who were fluent in English and under the age of 60 years were statistically more likely to feel responsible for their own safety and take an active role in their safety. Older male patients of lower education status are statistically less likely to question staff on hand hygiene. **Conclusion:** Despite numerous campaigns to improve patient involvement many patients are still not willing to participate

in their own safety. Patients without tertiary education, patients over 60, and those who are not fluent in English are much less willing to challenge healthcare professionals about safety-related issues such as hand-washing. Understanding the impact of patient demographics on participation in safety behaviours could help to create novel, more targeted strategies to improve patient safety. This could effectively reduce preventable medical errors in Obstetrics and Gynaecology.

OP2-411

SEQUENTIAL CERVICAL RIPENING - WORTHWHILE PROCEDURE OR DOUBLE TROUBLE?

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Problem statement: About 15-20% of the deliveries begin with an induction on labor. In cases of unfavorable cervical status, two major techniques are used for cervical ripening: mechanical interventions (e.g. balloon catheters) and pharmacologic agents, such as prostaglandins. Not uncommonly, an additional induction attempt is performed following the failure of a cervical ripening trial, whether by the same or by alternate method. However, no evidence was found in the literature regarding the success rates of sequential induction. In this study we aimed to examine this important issue. **Methods:** We performed a retrospective search for all patients undergoing induction of labor in Carmel Hospital between November 2014 and July 2018. Of these, only women who underwent two or more cervical ripening procedures (by double balloon catheter and/or Propess) were selected. Various demographic characteristics and obstetric outcomes were recorded. **Results:** Of the 874 cervical ripening procedures, 78 (8.9%) women underwent sequential induction. The majority were primiparous (59/78=75.6%), while three conducted a trial of labor after previous cesarean section. Of the 78 inductions, 70 (87.5%) women have entered the active phase of labor – 11/12 (91.7%) in two applications of Propess, 6/8 (75%) in two sequential insertions of double balloon catheter, and 53/58 (91.4%) in alternating methods. 21 (26.9%) deliveries ended in cesarean section, including 8 cases (10.3%) of failed induction. The rate of vaginal delivery did not statistically differ between various combinations of cervical ripening – 10/12 (83.3%) in two applications of Propess, 6/8 (75%) in two sequential insertions of double balloon catheter, and 51/58 (87.9%) in alternating methods. Four cases of postpartum hemorrhage were noted (5.1%), all in the alternating methods group. **Conclusion:** To the best of our knowledge, our study represents the first description of the outcomes of sequential cervical ripening. According to our results, it seems that following failure of one induction procedure, the majority of the women still can enter the active phase and achieve a vaginal delivery by using additional cervical ripening. These results can be used to reassure the patients in their way to successful delivery, as well as to encourage additional studies exploring this important subject.

OP2-501

IMMEDIATE POSTOPERATIVE PAIN CONTROL WITH ROPIVACAINE FOLLOWING LAPAROSCOPIC-ASSISTED VAGINAL HYSTERECTOMY: A RANDOMIZED DOUBLE-BLIND, PILOT STUDY

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Problem statement: Although laparoscopic hysterectomy, a worldwide popular surgery, ensures faster recovery and less postoperative pain than with laparotomic hysterectomy, immediate pain control still improving postoperative care. We introduce an



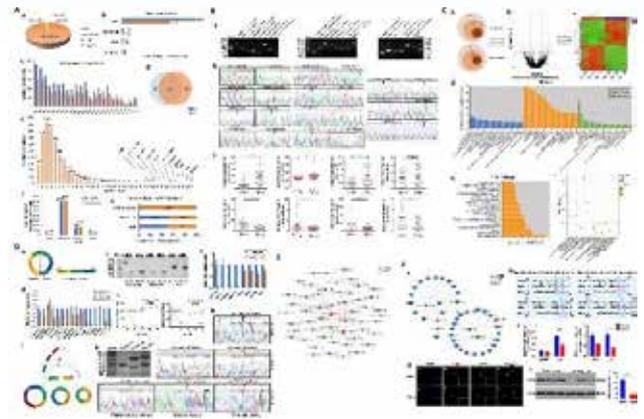
effective method, intraoperative injection of ropivacaine into both uterosacral ligaments, to control immediate postoperative pain. **Methods:** We performed a prospective, double-blind, and randomized study. We analyzed 40 cases of laparoscopic vaginal hysterectomy performed between July 2015 and November 2016 by a single surgeon (Y.S.K.). We randomized the enrolled patients into the ropivacaine injection group and the saline injection group. Before the vaginal stump was closed, 7.5% ropivacaine or saline (10mL) was administered into both uterosacral ligaments, 5 mL each. In all cases, the medicine was injected transvaginally before the vaginal stump was closed. The primary outcome was the postoperative pain intensity expressed by numeric ranking scale (NRS) scores at 2, 6, 12, and 24 h after injection. The secondary outcome was the amount of analgesics demanded for pain control during the 24 h after the surgery. **Results:** The pain intensity at 2 h after injection was significantly lower in the ropivacaine-injected group ($p = .0234$). There was no difference in pain intensity at 6, 12, and 24 h after injection and the amount of analgesics used. However, the total amount of opioid analgesic used was lower in the ropivacaine injected group than in the placebo-injected group. ($p = .0251$). **Conclusion:** Intraoperative ropivacaine injection into both uterosacral ligaments during laparoscopic hysterectomy can reduce early postoperative pain and consumption of analgesics to improve postoperative care.

OP2-502

IDENTIFICATION AND CHARACTERIZATION OF HUMAN OVARY-DERIVED CIRCULAR RNAs AND THEIR POTENTIAL ROLES IN OVARIAN AGING

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Problem statement: Circular RNAs (circRNAs) were recently shown to exert effects on multiple pathological processes by acting as miRNA sponges. However, the roles of circRNAs in ovarian senescence are largely unknown. The objective of this study was to identify the circRNAs involved in ovarian aging and predict their potential biological functions. **Methods:** We first performed RNA-sequencing to generate ovarian circRNA expression profiles from young ($n = 3$) and aging ($n = 3$) women with normal ovarian function. Biological function annotation was subsequently conducted using bioinformatics resources. We further validated the biological properties of ovary-derived circRNA by performing molecular biological experiments. A circRNA-miRNA-mRNA interaction network was constructed and preliminarily validated by qRT-PCR, immunofluorescence and western blotting. **Results:** In total, 48,220 circRNAs were identified, of which 194 circRNAs were significantly up-regulated and 207 circRNAs were down-regulated (fold change > 2 , $P < 0.05$). Bioinformatics analysis demonstrated that the metabolic process, regulated secretory pathway, oxidation-reduction process, steroid hormone biosynthesis, and insulin secretion pathways, which may be associated with ovarian aging, were significantly enriched ($P < 0.05$). The biological characteristics of ovary-derived circRNA, such as back-splicing, RNase R resistance, stability, and alternative splicing, were further validated. Bioinformatics predicted that most of the circRNAs harboured miRNA binding sites, of which circDDX10-miR-1301-3p/miR-4660-SIRT3 axis may be involved in the regulation of ovarian function. **Conclusion:** Our study indicates that circRNAs are aberrantly expressed in the aging ovary and may play potential roles in the development of ovarian senescence.



OP2-503

THE EFFECT OF THE HOT FLASH PROBLEM EXPERIENCED DURING MENOPAUSE ON COMPLEMENTARY ALTERNATIVE MEDICINE ATTITUDES AND HEALTH BELIEFS

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Problem statement: In the menopausal period, certain physical and mental changes related to lack of estrogen are seen in women, affecting their life negatively. According to study results, the most common problem seen among women in the menopausal period is hot flashes. Studies have shown that Hormone Replacement Therapy was found too high risk in coping with hot flashes, creating an increase in the trend towards complementary and alternative treatments. However, no studies examining the effect of the hot flash problem experienced during menopause on complementary alternative medicine attitudes could be found. **Aim:** This study was planned to determine the effect of the hot flash problem experienced during menopause on complementary alternative medicine attitudes and health beliefs. **Materials and Method:** The study was conducted in the gynecology polyclinic of an Obstetrics and Gynecology Research and Training Hospital tied to the Istanbul Directorate of Health between December 20th 2017 and April 30th 2018. 400 menopausal women meeting sample selection criteria were included in the study. **Results:** The mean age of the women included in the study was 51.14 ± 3.33 . It was determined that the most common problem experienced by the women participating in the study tied to menopause was hot flashes (88%), that 31.3% used complementary and alternative treatments to cope with menopausal symptoms, and that the most commonly used CAM method was prayer (90.4%). When the Holistic Complementary and Alternative Medicine Scale scores of the women who did and did not experience hot flashes were compared, the groups were found to be similar ($p > 0.05$), whereas when their Hot Flash Beliefs Scale and Menopause Rating Scale scores were compared, an advanced significant difference was found ($p < 0.001$). A positive, advanced significant relationship was found between the scores of the Menopause Rating Scale and the Hot Flash Beliefs Scale ($r = 0.43$; $p < 0.001$). **Conclusion:** Having hot flash problems in the menopausal period was found not to affect attitudes towards complementary and alternative medicine, whereas it was found to cause negative effects on hot flash beliefs and attitudes and indicate more severe menopausal symptoms.

OP2-504

IS OVARIAN CYSTIC LESION IS THE MOST FRUITFUL PATHOLOGY IN THE FEMALE INFERTILITY? – A SINGLE TERTIARY CARE CENTER EXPERIENCE

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Problem statement: To evaluate the success rate of the laparoscopic management of ovarian cystic lesions in term of the of the pregnancy outcome. **Methods:** We prospectively evaluated 157 female patients (age range 19-35 years; mean age 27.75 years) diagnosed as infertile, underwent hysterolaparoscopy during diagnostic work-up. Of these 157 patients, 61 patients (age range 20-34 years; mean age 27.0 years) were detected with the cystic ovarian disease with no other significant anatomical abnormality. All the recruited patients fulfilled the criteria of infertility; excluding male infertility, hormonal infertility and other causes of female pelvic anatomical abnormalities. The detected cystic ovarian anatomical abnormalities in the hysterolaparoscopy were tackled at the same time during diagnostic work-up if possible. After intervention we advised them for regular sexual activity and took the follow-up for 12 months at an interval of three months. **Results:** Of the 157 infertile female patients, 61/157 (38.9%) patients were detected as cystic (single/polycystic) ovarian disease on hysterolaparoscopic examination. Of these 61 patients, 41 (67.2%) were of primary infertility and remaining 20 (32.8%) patients were secondary infertility patients. Hysterolaparoscopy showed unilateral cystic disease in 9/61 (~14.8%) patients while bilateral cystic diseases in remaining 52/61 (~85.2%) patients. On ovary-based analysis, out of 122 ovaries (61x2), 96 were polycystic ovary, 17 were single cystic ovary and 9 were without cystic lesion. On 12 months follow up after the laparoscopic management of cystic lesions; 25/61 (41.0%) was conceived. The detected conceptions were distributed in 19/41 (46.3%) primary and 6/20 (30.0%) secondary infertility patients. There was the significantly higher conception rate ($p < 0.05$) in primary infertility patients than secondary infertility patients. On ovary-based analysis, 4/9 (~44.4%) patients with unilateral cystic lesion, 21/52 (40.4%) patients with bilateral cystic lesion were conceived. There was no significant difference ($p \sim 0.087$) in conception rate of unilateral and bilateral cystic lesion patients. **Conclusion:** We concluded that patient with the ovarian cystic lesions has significantly higher conception rate after the hysterolaparoscopic management in female infertility patients. Unilateral or bilateral cystic lesions do not affect the outcome of conception.

OP2-505

THE EFFECT OF SUFFICIENT AND INSUFFICIENT VITAMIN E IN TREATMENT OF INFERTILE PCOS PATIENTS

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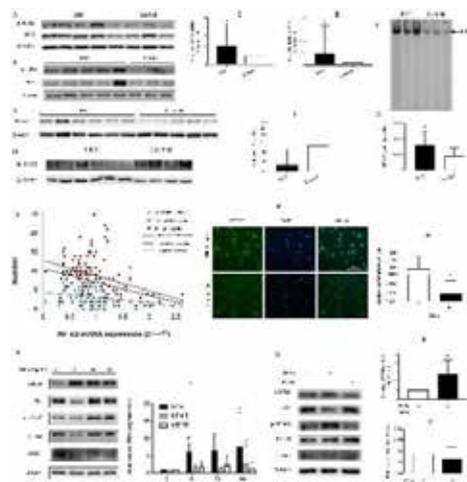
Objective: Vitamin E has multiple functions in humans and animals and its antioxidant effect was concluded in cancer therapy, high-risk pregnancy and male infertility. several investigators have demonstrated the benefits of dietary supplementation with vitamin E on fertility in different animal species. The aim of this study is to assess the effect of sufficient and insufficient levels of vitamin E on treatment of infertile PCOS women. **Methods:** In this clinical trial, 144 PCOS infertile patients referred to Dr. rasekh clinic, jahrom,iran that randomly divided in two groups (groups with

sufficient and insufficient levels). Each of these two groups was randomly divided into case and control groups (36 participants in each group). Usual drug regimen of PCOS started for all groups (Metformin and dydrogestrone). Case groups received vitamin E supplementation as an add-on their treatment. Data collection performed via questionnaires by midwives and statistical analysis by SPSS 21. **Results:** There was a significant relationship between follicular size and use of vitamin E ($P < 0.05$). Increased endometrial thickness and reduced BMI detected in using vitamin E group. The overall pregnancy rate was twenty women (66.7%) which related to the using vitamin E groups. **Conclusion:** Vitamin E has a positive effect on treatment of PCOS patients. Although response to the treatment is better in patients with insufficient vitamin E levels, prescription of this vitamin in patients with sufficient vitamin E level is also effective. According to rare side effects related to this vitamin, its low cost and low toxicity, we recommend to add daily use of vitamin E to drug regimen of infertile PCOS patients. key words: infertility, Vitamin E, pregnancy rate

OP2-506

THE FOLLICULAR ENVIRONMENT AND OOCYTE QUALITY OF WOMEN WITH OVARIAN ENDOMETRIOSIS: NUCLEAR FACTOR KAPPA B AND TELOMERASE OF GRANULOSA CELLS

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0.05 was considered statistically significant ($PD = 0.004$, $PE = 0.004$). (F, G) Levels of NF-κB-DNA binding were significantly higher in the endometriosis group. Column chart was quantitative comparison of NF-κB-DNA binding levels. * $P = 0.012$. (H) Protein expression of hTERT in GCs from endometriosis patient saw a downward trend. (I) GTA of patients with endometriosis was lower than controls, but not significantly ($P = 0.161$). (J) Distribution of the number of retrieval oocytes, mature oocytes, embryos available for transfer according to mRNA expression levels of NF-κB p65 in endometriosis GCs. Linear regression lines were drawn for retrieval oocytes (red line, $r = -0.339$, $P = 0.003$), mature oocytes (black line, $r = -0.403$, $P = 0.001$), and available embryos (blue line, $r = -0.27$, $P = 0.021$). Red circles indicated the number of retrieval oocytes, while black circles were for the number of mature oocytes and blue circles for available embryo number. (K) Increasing levels of TNFα significantly induced phosphorylation of IκBα and NF-κB p65 but decreased hTERT protein expression in cultured GCs. (L) TNFα at concentration of 50 ng/ml significantly increased mRNA



expression of I κ B α and NF- κ B p65. a, b, c Statistically significant compared with non-treated GCs (a* P 0.001, b* P 0.001, c* P = 0.031). (M) The effect of TNF α on immunofluorescent staining of hTERT in cultured GCs. Staining of hTERT (green), DAPI (blue) are shown (Scale bar, 20 μ m). (N) TNF α (50 ng/ml) significantly diminished TA levels in primary GCs (* P = 0.047). (O) PDTC decreased phosphorylation of I κ B α and NF- κ B p65 as elevated by TNF α . (P) The inhibition of NF- κ B pathway significantly increased mRNA expression of hTERT (* P = 0.007). (Q) GTA did not change significantly (P 0.05) after treated with PDTC. –, equal volume of PBS; +, 50 ng/ml for TNF α or 100 nM for PDTC. Each bar and column indicate standard deviation and mean. EMT, endometriosis; p-IKK β , phosphorylated IKK β ; p-I κ B α , phosphorylated I κ B α . **Problem statement:** Is telomerase activity (TA) associated with nuclear factor kappa B (NF- κ B) of granulosa cells (GCs) or intrafollicular inflammation of women suffered from ovarian endometriosis? Whether these changes might be related to oocyte quality of these patients? **Methods:** From February to December 2017, a total of 126 patients with ovarian endometriosis and 118 controls were enrolled in the Reproductive Medicine Center of Sun Yat-Sen Memorial Hospital. Cultured GCs were collected from another 45 controls. Intrafollicular concentrations of IL-6, IL-1 β and TNF α were measured with enzyme-linked immunosorbent assay (ELISA). NF- κ B binding levels were detected by electrophoretic mobility shift assay (EMSA). Modified quantitative-telomeric repeat amplification protocol assay (Q-TRAP) was performed for TA of GCs (GTA). The protein and mRNA expression were determined by quantitative PCR and Westerns, respectively. **Results:** Patients with endometriosis exhibited significantly lower number of antral follicle count (11.48 \pm 8.11 vs 15.68 \pm 8.56, P0.001), retrieved oocytes (8.28 \pm 6.69 vs 10.87 \pm 6.26, P0.001) and mature oocytes (6.67 \pm 6.09 vs 8.53 \pm 5.69, P=0.003) than controls. Inflammatory cytokines, such as IL-6, IL-1 β and TNF α , were compared between the two groups and did not differ significantly (P0.05). Compared with controls, GCs from endometriosis patients showed higher NF- κ B binding levels (P=0.012), increased mRNA expression of IKK β (2.743-fold, P=0.004) and I κ B α (5.017-fold, P=0.004). In women with endometriosis, GTA was negatively correlated to NF- κ B binding levels (r = -0.667, P=0.04987). Their mature oocyte number was also negatively associated with NF- κ B p65 mRNA expression ($b'_{NF-\kappa B}$ = -0.304, R^2 = 0.195, R = 0.442, P=0.018), which was positively associated with intrafollicular TNF α levels (R^2 = 0.14, r = 0.37, P=0.031). In cultured GCs, TNF α treatment significantly induced mRNA expression of I κ B α (5.408-fold, P0.001) and NF- κ B p65 (1.400-fold, P=0.031) but lowered hTERT expression and TA levels (0.0009 vs 0.5619, P=0.047); however, hTERT mRNA expression was obviously increased (1.988-fold, P=0.007) in the following use of NF- κ B inhibitor. **Conclusion:** Patients with ovarian endometriosis presented with activated NF- κ B signaling pathway in GCs, which might be a negative factor to GTA and oocyte quality. Intrafollicular TNF α might downregulate TA and hTERT of GCs via NF- κ B signaling pathway, but further studies are needed to confirm the regulation mechanism. 0.05 was considered statistically significant (PD = 0.004, PE = 0.004). (F, G) Levels of NF- κ B-DNA binding were significantly higher in the endometriosis group. Column chart was quantitative comparison of NF- κ B-DNA binding levels. * P = 0.012. (H) Protein expression of hTERT in GCs from endometriosis patient saw a downward trend. (I) GTA of patients with endometriosis was lower than controls, but not significantly (P = 0.161). (J) Distribution of the number of retrieval oocytes, mature oocytes, embryos available for transfer according to mRNA expression levels of NF- κ B p65 in endometriosis GCs. Linear regression lines were drawn for retrieval oocytes (red line, r = -0.339, P = 0.003), mature oocytes (black line, r = -0.403, P 0.001), and available embryos (blue line, r = -0.27, P = 0.021). Red circles indicated the number of retrieval oocytes, while black circles were for the number of mature oocytes and blue circles for available embryo number. (K) Increasing levels of TNF α significantly induced phosphorylation of I κ B α and NF- κ B p65 but decreased hTERT

protein expression in cultured GCs. (L) TNF α at concentration of 50 ng/ml significantly increased mRNA expression of I κ B α and NF- κ B p65. a, b, c Statistically significant compared with non-treated GCs (a* P 0.001, b* P 0.001, c* P = 0.031). (M) The effect of TNF α on immunofluorescent staining of hTERT in cultured GCs. Staining of hTERT (green), DAPI (blue) are shown (Scale bar, 20 μ m). (N) TNF α (50 ng/ml) significantly diminished TA levels in primary GCs (* P = 0.047). (O) PDTC decreased phosphorylation of I κ B α and NF- κ B p65 as elevated by TNF α . (P) The inhibition of NF- κ B pathway significantly increased mRNA expression of hTERT (* P = 0.007). (Q) GTA did not change significantly (P 0.05) after treated with PDTC. –, equal volume of PBS; +, 50 ng/ml for TNF α or 100 nM for PDTC. Each bar and column indicate standard deviation and mean. EMT, endometriosis; p-IKK β , phosphorylated IKK β ; p-I κ B α , phosphorylated I κ B α .

OP2-507

CORRELATION OF VISUAL (MODIFIED FERRIMAN GALLWAY SCORING) AND BIOCHEMICAL EVALUATION OF HIRsutISM IN POLYCYSTIC OVARY SYNDROME FILIPINO PATIENTS IN UERMMMC: A CROSS SECTIONAL STUDY

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Problem Statement: Polycystic ovarian syndrome (PCOS) is a common gynecologic endocrinopathy problem affecting 2.2% as high as 26% of population. They are usually presented with hirsutism and signs of ovulatory dysfunction. Hirsutism is the presence of excess body or facial terminal hair growth in females in a male-like pattern and is diagnosed through visual method, the Modified Ferriman Gallway (mFG) scoring system and biochemical tests, using total testosterone and free androgen index (FAI). The general objective of the study is to identify the correlation of visual scoring with the biochemical evaluation of hirsutism. Specific objectives include (1) to describe the visual and biochemical scores of hirsutism in PCOS patients and (2) to determine a cut off score for the visual scoring of hirsutism among Filipinos. **Methods:** This is a cross sectional study done at University of the East Ramon Magsaysay Memorial Medical Center (UERMMMC) in 2017. Ethical approval was obtained for this study. Patients who satisfied the inclusion criteria were included in the study. Age, height, weight, BMI and OB score were noted. Visual scoring for hirsutism using the mFG scoring system was performed. Blood extraction was done for testosterone and SHBG tests. Free Androgen Index was then computed and was correlated with the mFG scores. **Results:** A total of 52 patients were identified. A positive correlation is noted between the mFG with testosterone and FAI. A positive correlation was also noted between the BMI with testosterone and FAI. An mFG value of 4 is acceptable cut-off for Filipinos. **Conclusion:** The study showed as the mFG score increases, FAI and total testosterone level also increases. It was also noted that as BMI increases, the FAI and total testosterone level are also expect to increase. In can also be concluded that a lower mFG cut-off value, 4, is applicable for Filipinos.

OP2-508

URINARY INCONTINENCE IN PREGNANCY: A LITERATURE REVIEW

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Problem statement: Due to hormonal changes occurring in pregnancy, the capacity and neovascularization of bladder increase, while muscle tone of bladder and urethra decreases. Dilatation is seen in renal calyces and urethra, and some changes are observed in renal functions. An increase may be witnessed in stress urinary incontinence (SUI), because uterus puts pressure on bladder, especially in the last trimester, and increased relaxin hormone leads to relaxation in pelvic muscle and connective tissue.

Methods: Studies published in CINAHL, PubMed/MEDLINE and Cochrane Library databases were scanned to perform this review. The keywords were chosen from the MeSH list, and the following terms were defined: 'urinary incontinence' AND pregnancy AND 'pelvic floor' AND exercise. The reference lists from the selected studies were also scanned to identify other studies that could have been ignored. When literature was scanned through the key words, 95 studies in CINAHL, 142 in PubMed/MEDLINE and three in Cochrane Library database were encountered. Of these studies, only randomized controlled experimental studies were included into our review. **Results:** Pregnancy and delivery influence pelvic floor muscles negatively. To strengthen this muscle cluster, some methods, such as pelvic floor muscle exercises (PFME), strengthening abdominal muscles, biofeedback therapy, vaginal cones, sacral nerve stimulation, posterior tibial nerve stimulation and magnetic therapy. Pelvic floor exercises performed during pregnancy are known to reduce urinary incontinence during nearly postpartum one year. But it is uncertain whether antenatal PFME in incontinent women decreases incontinence in late pregnancy compared to usual care. In literature it is unclear whether antenatal PFME reduces urinary incontinence risk late postpartum.

Conclusion: Pregnant women need more health education and counseling about PFMEs. In light of the studies performed so far, the most beneficial approach to be recommended for women with pregnancy is to perform PFMEs and strengthen pelvic floor muscles during pregnancy and postpartum period in order to prevent urinary incontinence. However, we consider that PFMEs programmed sufficiently may be important for women at the risk of postpartum incontinence to prevent the condition. The effects of PFME may be greater with targeted rather than population-based approaches and in certain groups of women.

OP2-509

DO THE ANGIOGENIC AND HAEMOSTATIC PROFILES DEPEND ON TUMOUR'S LOCALISATION IN INVASIVE BREAST CANCER?

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Problem statement: Invasive breast cancer (IBrC) is more likely to develop in the left breast. The influence of tumour's laterality on prognosis is a matter of discussion. The aim of the study was to evaluate the association between tumour's localisation and clinicopathological features as well as selected haemostatic and angiogenic parameters: vascular endothelial growth factor A (VEGF-A), soluble vascular endothelial growth factor receptor 1 and 2 (sVEGFR1 and sVEGFR2), tissue factor (TF), tissue factor pathway inhibitor (TFPI) and plasminogen activator inhibitor-1

(PAI-1) in patients diagnosed with IBrC. **Methods:** Study group consisted of 92 women diagnosed with primary IBrC, without distant metastases. Mean age was 54.5 ± 7.5 years. Demographic and clinicopathological data such as tumour characteristics, surgical procedures, lymph node count and metastatic lymph nodes were collected. The exclusion criteria were as follows: bilateral IBrC, male gender, incomplete histopathology report, previous radiotherapy or chemotherapy, recent bleeding or thrombotic events. Haemostatic and angiogenic parameters were performed applying enzyme-linked immunosorbent assay (ELISA) with a commercial kit. **Results:** IBrC was slightly more frequently found in the left breast, however the difference was not significant ($p=0.8542$). The most common molecular subtype of IBrC – luminal A was more likely to be found in the right breast. However, other molecular subtypes of IBrC – luminal B, triple negative or HER2+ - were significantly more likely to develop in the left breast. Breast cancer laterality was also associated with HER2 expression ($p=0.0357$) where 9 left-sided tumours had overexpression of HER2 and in right-sided tumours only one patient had positive score. Patients with tumour in the left breast were characterized by significantly higher concentrations of VEGF-A, PAI-1 and lower anti-angiogenic potential expressed by sVEGFR2/VEGF-A ratio, compared to patients with tumour in the right breast. TFPI activity was higher in patients with tumour in the left breast, the difference was close to significant value ($p=0.0985$). Tumour's localisation was not associated with TF levels. **Conclusion:** Altered levels of examined factors indicate increased activation of angiogenesis and decreased fibrinolytic activity in patients with tumour in the left breast, what may be associated with worse prognosis in this group.

OP2-210

Testis Regenerative Matrix (TREM) bioexpansion in Testis Insufficiency Syndrome (TIS)

Testis Expandable BioSurgery and MicroSurgery (TEBS and TEMS) in Male Infertility based on Autologous Regenerative Stem Cells

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In the last COGI Congresses in Paris (Paris, France, November 17-20, 2011, A6), in Hainan (Hainan, China, December 8-11, 2011, A27), in Singapore (Singapore, July 19-22, 2012), in Wien (November 30-December 2, 2017) innovative TREMS Technologies (TREMS – Technology for REproductive Medicine and Surgery) have been presented for MARS (MAle Reproductive Surgery and MicroSurgery). Testis Expandable BioSurgery and MicroSurgery (TEBS and TEMS) based on Cell Technology (Reproductive Cellomics) and on natural autologous Nanosomes (SpermoSomes) are designed for Testis Insufficiency Syndrome (TIS) in Male Infertility and in Andropause. The Testis Insufficiency (Impairment) Syndrome – TIS is defined on 3T Parameters: Temperature Increasing, measured by IR Technology; Testosterone Decreasing, measured with salivary test; Testis Function Impairing, measured by computer-assisted Dynamic Imaging Technology (Power Doppler Ultrasound and Raman Spectroscopy). A flagship multi-centric clinical trial is realized on 85 cases of TIS Syndrome to implement a new procedure for Testis Matrix Regeneration using Autologous Mesenchymal Stem Cells with a follow-up of 1 year and half. The TREM Expansion in TIS has been realized with the technique TAS (Testis Augmentation Surgery) using a vascularized island vaginalis flap to enlarge the testis with the goal to transform the testis ovoid from Dixon Euclidean eggs classes to Golden Egg standard. Through the albugineal incision a microprobe tunneling the interlobular spaces has been used to permit the injection of microplugs of samples of purified adipose regenerative stem cells extracted from the same fat tissue of the patient from the abdomen or from the scrotum. The samples of regenerative stem cells were activated before introduction into a special box delivering ultrasound cavitation multispectra low frequencies through a SHDB Cell System for 20 minutes. The volume of the testis and the blood level of testosterone are the basic parameters monitored during the period of follow-up. The volume of the testis increases of more than 20 per cent with a normalization of the ovoid into the Dixon categories and a real improvement of the power doppler parameters. The level of blood testosterone increases in a period of 6 months from a mean value of two measurements of 2.45 ± 0.47 to 4.50 ± 0.82 . The New Advanced Expandable MicroSurgery Techniques on the Human Testis (TEMS) to enhance or repair or regenerate the Intertubular Matrix of the Human Testis through Autologous Mesenchymal Stem Cells (Cell Therapy) represent the first attempt to reverse the hypogonadic status of the male gonads. Clinically Evaluable Male Factor Restoration and Improvement and Social Economy Benefits are described comparing and addressing Human Reproduction and Family Welfare Policies in Western and Asian Countries.



POSTER ABSTRACTS

ART/IVF

P001

EVALUATION OF THE RECEPTIVITY OF THE ENDOMETRIUM ON THE BASIS OF INTEGRAL ANALYSIS IN PATIENTS WITH INFERTILITY IN ART PROGRAMS

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Problem statement: To study the effect of endometritis on the implantation implementation, a study of gene expression in the transcriptome format morphometric analysis of histological sections of was conducted to search for diagnostic markers of chronic endometritis during the "implantation window" with problems associated with infertility. We examined 33 patients with tubal factor infertility, which were divided into 2 groups: 1 group was represented of 15 women with plasmocytes in endometrial scrapings during the proliferation phase; the second group was represented of 18 women without plasmocytes in endometrial scrapings during the proliferation phase. **Methods:** Mathematical methods of pattern recognition for image analysis (microphotographies of histological sections of the endometrium) and multidimensional mathematical methods of data analysis (NMF- Non-negative matrix factorization) were used to obtain information on the dynamics of molecular and morphological processes in endometrial tissue during regeneration. Morphological methods included IGH research. We also applied analysis of the expression level several target genes by quantitative RT-PCR. **Results:** A new, independent informative marker, VEGFA, was discovered, which makes it possible to diagnose the presence of CE (chronic endometritis) in the second phase of the cycle. Increase in mRNA expression of the VEGFA gene in the middle stage of the secretion phase is associated with the presence of plasmocytes in the 1st phase of the menstrual cycle. If plasmocytes are present in the endometrium of the middle stage of the secretion phase the mRNA expression of VEGFA genes increases 1.7 times, VEGFA189 -by 2.4 times, IGFBP1 -16.6 times, CD68 – 2 times, and also expression of the mRNA of gene IL2 decreases - 1,5 times in comparison with patients with the absent of plasmocytes in the endometrium. **Conclusion:** The newly discovered marker provides early diagnostics of early stages of endometritis and as a consequence may increase the effectiveness of ART programs.

P002

A MULTI-DOSE, PREFILLED PEN INJECTOR FOR THE ADMINISTRATION OF FOLLITROPIN ALFA WITH A DOSE INCREMENT OF 5 IU

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Problem statement: Patients undergoing treatment for infertility are often prescribed subcutaneous injections of follicle-stimulating hormone (FSH), which is to be administered with precise and convenient pen injectors. Nomograms for the precise calculation of the FSH starting dose were developed based on factors such as antral follicle count and serum anti-mullerian hormone. New pen injectors are needed to allow for the accurate self-administration of FSH in a wide range of starting doses with a dose increment lower than that of existing injectors. The new follitropin alfa pen injector is designed with a dose range of 0 to 300 international units (IU) and a dose increment of 5 IU. **Methods:** In this study, 48 pen injectors were tested, each having a pre-installed cartridge size of 300 IU. Three dose dial settings - minimum (5 IU), midrange (150 IU), and maximum (300 IU) – were tested in compliance with ISO 11608-1:2014(E) for each pen injector. **Results:** Testing the 48 pen injectors produced the following results: for the estimated minimum dose of 5 IU (target dose: 0.0083 ml) the mean value of the dispensed volume (X) was 0.0081 ml, and the mean deviation (SD) was ± 0.0006 ml; for the midrange dose of 150 IU (0.2499 ml), X= 0.2478 ml and SD= ± 0.0030 ml; for the maximum dose of 300 IU (0.4990 ml), X= 0.4941 ml and SD= ± 0.0062 ml. The results are consistent with the ISO 11608-1:2014(E) requirements of dose accuracy: for N = 48 pen injectors, coefficient K_{tar} =2.736 (two-sided tolerance p=0.975, 95% confidence level) should be less than estimated coefficient K_{act} for each dispensed dose (K_{tar} K_{act}). For the minimum, midrange, and maximum doses, K_{act} is 9.94, 3.45 and 3.24, respectively. The described pen injector is currently being used in the ongoing clinical study of the equivalence in women undergoing IVF/ICSI (NCT 03088137). **Conclusion:** The personalized approach to the follitropin alfa starting dose selection (based on individually-estimated physiological parameters) and the minimum dose adjustment increment of 5 IU may help achieve an accurate adjustment of the required dose of follitropin alfa for ovarian hyperstimulation and ovulation induction protocols.

P003

BENEFICIAL EFFECT OF AUTOLOGOUS ENDOMETRIAL STROMAL CELL CO-CULTURE ON DAY 3 EMBRYO QUALITY

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Problem statement: One of the factors associated with poor success rates in human IVF is the suboptimal culture conditions in which fertilization and early embryonic growth occurs. Co-culture systems with helper cell lines appear to enhance the in vitro conditions and allow embryos to demonstrate improved development. The study aimed to examine the influence of autologous endometrial stromal cell (EnSC) co-culture on day 3 embryo quality by comparing the morphological status of the embryos from the same patients undergoing consecutive IVF/ICSI cycles without and with EnSC co-culture. **Methods:** This study includes 20 couples and a total of 46 IVF/ICSI cycles. Each patient couple had at least two IVF/ICSI procedures – one with and one without autologous EnSC co-culture. Embryo quality was assessed at 68±1 hours in culture, according to Istanbul consensus criteria (2010). Day 3 embryos were classified into three groups: good – grade 1; fair – grade 2; poor – grade 3. Embryos from all cycles were divided into two groups (A – co-cultivated; B – not co-cultivated) and analyzed. Second, for each patient couple, embryos from matched IVF/ICSI cycles (with and without co-culture) were analyzed separately. **Results:** When an analysis of co-cultivated day 3 embryos from all cycles was performed (n=137; group A), 43.1% of the embryos were graded as "good", which was not significantly different from the respective embryo quality rate of 42.2% (p=NS) in group B (n=147). The proportions of fair and poor quality embryos in group A and group B were similar as well –

11.7% vs 10.2% and 45.2% vs 47.6% (p=NS), respectively. The separate embryo analysis by matched cycles for each couple revealed that in 65% of the cases the proportion of morphologically better embryos was increased in cycles with co-culture. A decrease in this proportion after EnSC co-cultivation was found in 30% of the cases. **Conclusion:** The results demonstrated that there is no marked difference in the overall morphological quality between co-cultured and non-co-cultured embryos on day 3. However, in significantly greater percentage of couples the process of autologous EnSC co-culture could increase the proportion of morphologically improved day 3 embryos.

P004

THE INFLUENCE OF EARLY FOLLICULAR PROGESTERONE LEVEL ON PREGNANCY RATE IN GnRH ANTAGONIST IVF/ICSI CYCLES— HOW HIGH IS TOO HIGH?

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Functional luteolysis that occurs at the end of menstrual cycle is characterized by reduced progesterone (P) production, which reaches its nadir at menstruation. Significantly higher P levels in the early follicular phase of a spontaneous cycle have been demonstrated in women who had a poor response during a IVF treatment, and it is considered to be a possible indicator of ovarian aging. Despite the intervention strategies to treat patients with elevated early follicular P levels, pregnancy rates remained lower in the patients with high early follicular phase P level compared with the patients with the normal P. **Study design:** The prospective, cohort study included 94 infertile patients treated by IVF/ICSI at the Department of Human reproduction, University Hospital Centre Sisters of Mercy. The study period went from April 2017 to October 2017 (6 months). **Participants and methods:** Patients undergoing their first GnRH antagonist IVF/ICSI cycle, aged 26-42, BMI 30 kg/m². On 2nd day of spontaneous menstrual cycle the levels of progesterone and anti-Mullerian hormone (AMH) were measured. The patients were divided in 2 groups. The first group consisted of women who had P values of 1.0 ng/L ("low normal values") while the second group consisted of women with progesterone values of 0-1.6 ng/L ("high normal values"). **Results:** The total of 94 women aged 26-42 in whom the basal P levels on day 2 of menstrual cycle were ≤ 1.6 ng/ml (5.1 nmol/L) were analyzed. The P levels 1.0 ng/L ("low normal values") was found in 84 women (89,36%) and 1.0-1.6 ng/L ("high normal values") in 10 women (10,64%). Out of 94 patients, 32 of them had positive pregnancy test (pregnancy rate (PR) 34.0 %). In first group PR was 36.9%, whereas in second group only 10%. Statistically significant difference between these two groups was estimated (36.9% vs 10%, p=0.08). No statistically significant difference in age (35.5 vs 35.2, p=0.41) or in AMH levels (18.3 pmol/L vs 19.6 pmol/L, p= 0.43) was found. Results were evaluated statistically using SPSS 17 (IBM, NY, USA).

P005

OUTCOME VARIABLES IN AN ART CLINIC OPERATING UNDER RESTRICTIVE REGULATIONS

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Problem statement: The main ART clinic within the NHS unit in Malta has been operating since 2014. During this time period, various alterations to the current practice have been carried out in attempt to improve fertility outcomes. **Methods:** All the 25 cycles since January 2014 till July 2018 were analysed for various outcome variables including type of cycle used and pregnancy outcome to investigate whether it is possible to achieve acceptable

success rates in an environment operating under restrictive regulations. The cohort was divided into broad categories mainly those undergoing fresh cycle and those using frozen eggs. Patient pathology was classified according to reason for infertility - male, female, both or unexplained. **Results:** Of the 789 couples who underwent an IVF/ICSI cycle during the mentioned time period, 648 underwent a fresh cycle, and 141 underwent a frozen cycle, some of which were repeated cycles. The average age of females undergoing treatment was 35 years while that of males was 37 years. Pregnancy outcomes including biochemical pregnancy obtained, live birth rate, gestational age at delivery, mode of delivery and any fetal anomalies recorded were analysed. **Conclusion:** Overall outcomes were better in the fresh cycles when compared to the frozen cycles. Of all the pregnancies obtained, 18 were multiple pregnancies. Most pregnancies carried to term, with minimal complications antenatally and postnatally.

P006

CLINICAL OUTCOME OF DAY 3 VITRIFIED-THAWED EMBRYO COMPARE WITH DAY 5 VITRIFIED-THAWED BLASTOCYST

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Introduction: Introduced in 2000, the embryo vitrification technique has brought important benefits for IVF therapy. It allows the embryo freezing at any stage and results in higher survival, pregnancies and live birth rates from the frozen-thawed embryo transfer cycles. The study compare the clinical pregnancy rate between day 3 cleavage stage and day 5 blastocyst vitrified-thawed embryos. **Materials and Methods:** The 1-year study included 79 FIV autologous with embryos vitrified and thawed. Of these 27 patients received day 3 vitrified-thawed embryos and 52 patients received day 5 vitrified-thawed embryos. The results were statistically analyzed. **Results:** The study included 64 day 3 vitrified-thawed embryos out of which 61 embryos survived and 101 vitrified-thawed day 5 embryos of which 97 embryos survived. The embryo survival rate after thawing was not significantly different: 95.31% in the first case and 96.04% in the second case (P=0.75). Clinical pregnancy rate per cycle transfer was significantly higher in vitrified-thawed blastocyst transfer compared to cleavage-stage vitrified-thawed embryo transfer (46.15% vs. 29.62%, P0.05). **Conclusions:** This study is a retrospective study that demonstrates that subsequent vitrified-thawed blastocyst transfer in a non-controlled ovarian hyperstimulation cycle dramatically improves clinical outcomes. Therefore blastocyst culture in tandem with vitrified-thawed blastocyst transfer is recommended as a favorable and promising protocol in human IVF.

P007

ARE IVF PREGNANCIES HIGH RISK PREGNANCIES AFTER 28 WEEKS?

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Introduction: A study done to determine whether the complication rate in IVF pregnancies is different from that in the background control population. **Methods:** A number of specific complications were looked at. All pregnancies from a major NHS hospital were collected over a 2 year period. Successful IVF pregnancies were followed up after 28 weeks gestation and compared to a matched cohort of pregnant controls. A number of maternal complications including diabetes, hypertension, pre-eclampsia, antepartum hemorrhage and multiple pregnancy, were looked at. Fetal outcome with regards to weight at birth and anomalies were also noted. Complications that could have complicated the pregnancy,



such as placental abruption, placenta previa and intrauterine death were also assessed. **Results:** Given the high risk nature of the IVF population, age, weight, reproductive pathologies and other factors, it is often assumed that the pregnancies tend to be high risk. Our results show a trend that suggest that this may be so and that previous conclusions from other studies are corroborated. **Conclusion:** The possibility of high risk pregnancy should be part of the counselling that patients are offered prior to undertaking IVF treatment. Being aware of these potential complications one can employ early interventional measures can be undertaken early in the pregnancy period so that their effects on the outcome is minimised.

P008

FEASIBLE INFLUENCE OF CSGF ON PREGNANCY OUTCOME FOR NON-IMPLANTIVE EGG DONATION CYCLES

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Problem statement: To study whether uterine lavage of colony-stimulating growth factor (CSGF) on the day of egg collection (EC) influence the pregnancy outcome in egg donation (ED) cycles for patients with recurrent implantation failure (RIF). **Methods:** Randomized-controlled trial, pilot study. Enrolled 110 subjects with RIF were randomized into two arms: control and experimental – 74 and 36 subjects in each correspondently. The average age in the experimental arm was 43.9 year in comparison to 41.8 year in the control arm (t=3.24 p=0.0016). Body mass index 23.1 kg/m² in experimental and 23.9 kg/m² in the control arm (t=0.8 p=0.4260). Study period was 12 months. We divided the causes of RIF into two large groups, the first one – morphological embryo quality and its genetic competence and the second – endometrial factor. We presume to exclude the influence of embryonal factor upon the implantation rate because all subjects underwent ED cycles with good quality embryos. Inclusion criteria were: present ED cycle, at least one failed ED cycle with the good quality embryos (Gardner scale) and several unsuccessful cycles with own genetic material, absence of severe male factor and absence of uterine pathology. In both arms endometrial thickness on ET- 5days was 7.0 mm in experimental and 8.0 mm in control (t= 6.42, p=0.00001). Experimental arm underwent uterine lavage with 0.3 mg CSGF (Wallace ET catheter) on ET- 5 days, while control arm remains not. There was no significant difference in number of transferred embryos in both arms: 1.73 in control and 1.83 in experimental. **Results:** Endometrium thickness measured on ET day remains unchanged 8.01 mm control arm in comparison to 8.25 mm in experimental arm (t=1.56, p=0.1210), so it increased on 1.25 mm (7.0 mm to 8.25mm t= 6.87 p=0.00001 – statistically significant). Pregnancy rate (PR) was 43.2% in control arm comparable to 58.3% in experimental arm (t=1.50 p=0.1357). Difference of PR is insignificant due to small number of subjects in the pilot study.

P009

TERMOGRAPHY AND OOCYTE & EMBRYO SURVIVAL RATES

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Problem statement: The first step in the oocyte/embryo devitrification procedure by the Kitazato® method consists in immersing the cryotop in the Thawing Solution (TS) for a minute at 37°C. Preheated aluminum warming plates (WPs) are used in order to keep the 37°C as constant as possible. By means of thermography it was observed that the temperature (T) decreased more slowly if adhesive silicone blocks were used glued to the WP (WPSB), acting as a thermal insulator as we could see in previous investigations (IX ASEBIR Congress, 2017). The main key of study

is to compare the oocyte survival rate (OSR) according to the material that was used to maintain the T of the oocytes (WP or WPSB) and the secondary objective of study is to compare the embryo survival rate (ESR) according to the use of WP or WPSB. **Methods:** This retrospective cohort, observational and unicentric study at IVIRMA IVI-Madrid was performed between 1 May, 2015 and 31 December, 2017. The study included two fourteen-month-periods for each group which contained patients and donors who devitrified their oocytes/embryos. The two groups were: WP group and WPSB group. A total of 15225 and 13408 devitrified oocytes were respectively analyzed. And a total of 3963 and 4324 devitrified embryos were respectively analyzed.

OOCYTES	Survival	Not survival	Sum	P value – χ^2
WP	12289 80.58%	2956 19.42%	15225	<0.0001
WPSB	11307 84.33%	2101 15.67%	13408	
Sum	23576	5057	28633	
EMBRYOS	Survival	Not Survival	Sum	P value – χ^2
WP	3673 92.68%	290 7.32%	3963	0.1938
WPSB	4040 93.43%	284 6.57%	4324	
Sum	7713	574	8287	

P010

UNDERSTANDING REPRODUCTIVE IMMUNE STATUS OF PATIENTS WITH RECURRENT IMPLANTATION FAILURE FROM THE ASPECTS OF AUTOIMMUNE AND COAGULATION FUNCTION

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Problem statement: To determine the prevalence of autoimmune and coagulation disorders in women with recurrent implantation failure (RIF), and compare the prevalence after excluding anatomical, endocrinological, endometrial and genetic disorders. **Methods:** 296 non-pregnant women with recurrent implantation failures after IVF/ET procedures were tested for peripheral blood autoimmune and coagulation profiles. The prevalence of markers of autoimmune and coagulation function was compared before and after aetiological screening. **Conclusion:** Among all RIF patients, 34.44% demonstrated at least one positive autoimmune marker, and 45.16% at least one coagulation marker. After excluding anatomical, endocrinological, endometrial and genetic disorders, the rate of at least one positive autoimmune marker increases to 39.02%, and 44.74% for coagulation marker. Autoimmune disorders may play a role in recurrent implantation failure, and the use of immunosuppressive or anticoagulant drugs as adjuvant treatment need further studies.

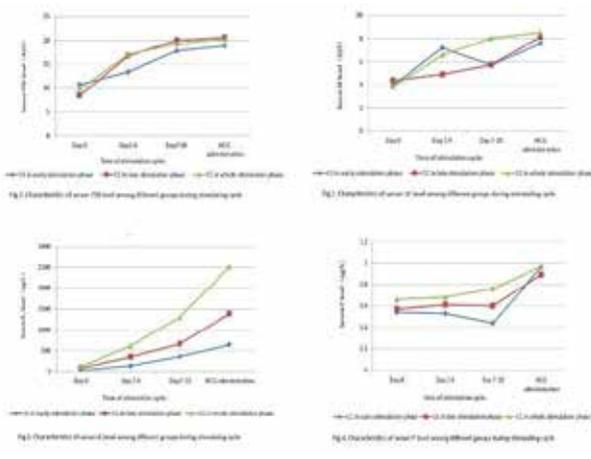
Examination	Abnormality rate before screening	Abnormality rate after screening
Blocking antibody (-)	76.36%	73.68%
Natural killer cell(-)	74.70%	70.73%
Platelet aggregation function(-)	64.04%	38.89%
Anti-thyroglobulin antibody(-)	26.78%	45.00%
Anti-thyroid peroxidase antibody(-)	26.78%	35.00%
Antinuclear antibody (+)	22.06%	23.08%
Anti-β ₂ -glycoprotein I antibody (+)	13.64%	7.89%
Protein C(-)	11.32%	18.52%
Antithrombin III activity(-)	9.02%	4.76%
Anti-dsDNA antibody (+)	8.82%	0.00%
Anti-α ₂ -Fodrin A antibody (+)	8.11%	0.00%
Protein S(-)	7.55%	7.41%
Anticardiolipin IgG antibody (+)	6.67%	5.26%
Anti-C1q antibody (+)	4.41%	7.69%
Anti-nucleosome antibody (+)	2.94%	0.00%

P011

CHARACTERISTICS OF SERUM GONADOTROPIN PROFILES IN ELDERLY POR PATIENTS WITH CLOMIPHENE CITRATE TREATMENT UNDERGOING IVF/ICSI

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Problem Statement: Based on economic benefits, mild stimulation protocol with clomiphene citrate (CC) is an option for poor ovarian response (POR) patients, when they failed to achieve desired outcome with conventional protocols. Generally, three protocols of CC administration are as followed. (1) CC in early stimulation phase: patients received CC on day 1-5 of the cycle for 3-5 days then received exogenous gonadotropin (Gn) instead. (2) CC in late stimulation phase: After initiation by Gn, patients received CC according to luteinizing hormone (LH) level until the day of HCG injection. (3) CC in whole stimulation phase: patients received CC throughout the whole cycle, whether Gn is used or not. This study aimed to clarify the effectiveness of CC for elderly POR patients undergoing IVF/ICSI. **Methods:** 290 POR patients (≥ 35 y) undergoing mild stimulation protocol with CC were included into this retrospective analysis. Endocrine profiles including Serum FSH, LH, estradiol (E_2) and progesterone (P), and clinical outcome including oocyte retrieval would be compared between different groups divided by age and protocols. **Results:** (1) Overall, CC could increase serum FSH level and LH level which subsequently stayed in a high level. Oocyte retrieval rate (number of patients who obtained oocytes/ number of all patients) reached 92.1%. Cycle cancellation rate was 87.3%, of which 46.9% was due to thin endometrium. (2) There was no significant difference in endocrine profiles and clinical outcome among different age groups (35-38y, 39-42y and ≥ 43 y). (3) No significant difference was found in serum FSH level and LH level between different CC protocols. When CC was used throughout the stimulation phase, serum E_2 level evidently higher than the other two groups from the 3rd-6th day of stimulation cycle to the day of HCG injection. In that group, E_2 level per oocyte, oocyte retrieval rate, the number of oocyte retrieved and mature oocyte were also higher ($P < 0.05$). **Conclusion:** For elderly POR patients, CC can effectively increase serum FSH levels thus initiate follicular recruitment. Meanwhile serum LH levels rise and maintain in a high level without LH surge. The use of CC throughout the cycle can reduce follicle escape and has economic advantages.



P012

INTRAUTERINE INSEMINATION – PREDICTIVE FACTOR FOR SUCCESSFUL OUTCOME IN THE PORTUGUESE SETTING

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Problem statement: Infertility is a disease that affects millions of people worldwide. World Health Organization refers to it as public health problem with strong individual, demographic and economic implications. The advent of medically assisted reproduction was one of the great breakthroughs in the field, and it is crucial to join efforts and resources towards the study and optimization of the techniques, such as the intrauterine insemination procedure. The authors report the success rate of the intrauterine insemination cycles performed at our Unit and the predictive factors of success.

Methods: This is an observational, analytical and retrospective study. The target population refers to intrauterine insemination cycles performed at our Unit between January 2013 and December 2016, with a total sample size of 126 cycles, resulting in 113 cycles of insemination to further analyze. **Results:** It was observed that out of the 113 cycles under study, the most frequent age group in both partners was 30-34 years old (60,2% in women, 49,6% in man). A great fraction of women had a body mass index (BMI) less than 25 (68,8%), had no relevant clinic history (35,7%), didn't display changes in the pre-insemination ultrasound evaluation (79,5%) and had an endometrial thickness equal or greater than 8 mm (73,2%) at the time of the procedure. In most cases, none of the partners is a smoker (66,4%). An overall success rate of 20,4% was achieved, resulting in a positive Beta HCG test. **Conclusions:** In this study, the pregnancy rate obtained from intrauterine insemination was 20,4%. In the literature, pregnancy rates found are quite broad, since the features of each study and sample strongly influence the results. Therefore, the predictive factors of pregnancy were evaluated and a higher success rate is associated with younger women. No statistical evidence was detected among the other studied variables. Disclosure of interest The authors report no potential conflict of interest to disclose. Keywords infertility, assisted reproductive technology, intrauterine insemination

P013

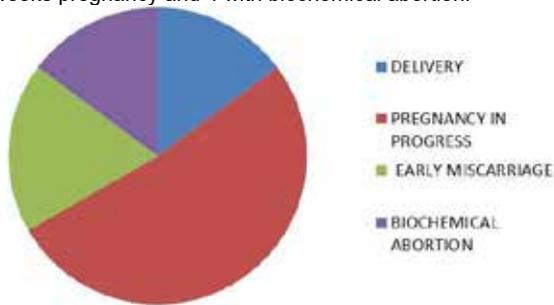
USE OF ENDOMETRIAL PRP (PLATELET RICH PLASMA) WITH PLATELET DEGRANULATION IN TREATMENT OF PATIENTS WITH FAILED IVF ATTEMPTS

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Problem statement: PRP is a new promising regenerative therapeutic application which can offer therapeutic benefits without detrimental side effects as it is a direct product of own blood sample. PRP has been employed in several fields of medicine: from plastic surgery, maxillo-facial surgery, dental surgery, orthopedics, eye surgery and gynecology. PRP is highly rich in several growth factors that have a significant role in tissue regeneration. The main ones include epidermal growth factor, vascular endothelial growth factor, transforming growth factor beta 1 and beta 2, interleukin 10, several classes of platelet-derived growth factors. More recently, clinical trials have provided substantial amount of evidence that PRP can have many beneficial effects in the field of infertility through its regenerative effects. PRP applications have been demonstrated to have cell proliferative



effects as well as anti-inflammatory effects while working on tissue repair. PRP application has also been associated with increased progesterone receptor activity. Progesterone receptors are the main actors that help maintain a thick and healthy endometrial lining, which in turn, helps with embryo implantation. **Methods:** We have started offering PRP applications for 84 patients with: adenomyosis, previous IVF failures and patients who cannot obtain a desired level of endometrial thickness for a successful embryo transfer. The endometrial PRP application is administered approximately 48-96 h before embryo transfer. PRP was prepared from autologous blood using RegenACR kit according to manufacturer's instructions and subsequently infused on the endometrium using Gynetics catheter. **Results:** After application of PRP, the endometrial thickness was satisfactory in all patients (>8 mm), with endometrial three-layer pattern, before progesterone administration and embryo transfer was performed; of these patients with previous IVF failures beta-HCG was positive in 28 of them: 4 live-birth following a delivery of healthy baby, 14 women with physiological pregnancy, 6 had early miscarriage within 12 weeks pregnancy and 4 with biochemical abortion.



Conclusion: In our experience, PRP treatment seems to have an important regenerative function, because all patients subjected to treatment had a good endometrial thickness, ideal for embryo implantation. These results translates into several pregnancies, registered also in women with previous IVF failures.

P014

USE OF PRP (PLATELET RICH PLASMA) WITH PLATELET DEGRANULATION IN OVARIAN REJUVENATION FOR FAILED IVF ATTEMPTS AND POOR RESPONDER PATIENTS

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Problem statement: PRP is a new promising regenerative therapeutic application which can offer therapeutic benefits without detrimental side effects as it is a direct product of own blood sample. PRP has been employed in several fields of medicine: from plastic surgery, maxillo-facial surgery, dental surgery, orthopedics, eye surgery and gynecology. PRP is highly rich in several growth factors and so it have cell proliferative effects as well as anti-inflammatory effects while working on tissue repair. The main ones include epidermal growth factor, vascular endothelial growth factor, transforming growth factor beta 1 and 2, interleukin 10, several classes of platelet-derived growth factors. More recently, clinical trials have demonstrated that PRP can have many beneficial effects in the field of infertility through its regenerative effects. Autologous ovarian PRP treatment could result in successful management of poor responders patients with failed IVF attempts, poor oocyte yield and poor embryo quality. **Methods:** We have started offering ovarian PRP applications for 27 patients between 40 and 45 years old with: IVF failures, poor oocyte yield and POF (Premature Ovarian Failure). Ovarian PRP is programmed approximately in 8-10 day of menstrual cycle. PRP was prepared from autologous blood using RegenACR kit

according to manufacturer's instructions and subsequently 1 cc of PRP was infused on ovaries using a 20-21 G needle under transvaginal ultrasound guidance. We was used different concentrations of PRP according to the level of ovarian hyporesponsiveness. **Results:** Following PRP treatment, patients were monitored by both ultrasound and hormonal profile and following their upcoming menstrual cycle, ovulation and presence of follicle: 5 of these patients with AMH between 0.2-0.4 and previous IVF failures achieved pregnancy. **Conclusion:** To verify action of this treatment we attach importance to presence of dominant follicle in 8-10 day of cycle; we also check the hormonal profile of FSH and E2 in 3rd day of menstrual cycle. The results of ovarian PRP are promising because 20 patients of 27 achieving a regular ovulation within 6 months of the treatment: 5 of them realized physiological pregnancy and 1 of them resulted in a successful live-birth following caesarean section of a healthy girl.

P015

FRESH VERSUS FROZEN-THAWED EMBRYO TRANSFER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PERINATAL OUTCOMES

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Problem Statement: Fresh embryo transfer (ET) may be associated with poorer perinatal outcomes due to altered implantation, decidualization, and placentation in pregnancies after a controlled ovarian stimulation. Lower risks of preterm birth, small for gestational age (SGA) and low birth weight (LBW) were found in pregnancies after frozen embryo transfer (FET) compared with singletons conceived after fresh ET. Study question: In patients undergoing assisted reproduction techniques with FET, are there differences in perinatal outcomes versus those with fresh ET?

Methods: Design: Systematic review and meta-analysis of cohorts studies, Case-control studies, RCT Patients: Women submitted to Assisted Reproductive Technology. An electronic literature search in Pubmed, MEDLINE and Cochrane Central Register of Controlled Trials was performed. Main outcomes: Preterm birth, LBW, Very low birth weight, Large for gestational age (LGA), SGA, Mean gestational age, Mean Birth weight, Perinatal mortality, Macrosomia. **Results:** A cohort of 151706 pregnancies conceived after FET versus 404263 with a fresh ET was evaluated. 29 studies met inclusion criteria. FET is associated with a lower risk of preterm birth (OR = 0.88 95% CI 0.80-0.97), SGA (OR = 0.61 95% CI 0.58-0.64), LBWR (OR = 0.71 95% CI 0.67-0.76) and VLBW (OR = 0.75, 95% CI: 0.66-0.87). There was no significant difference in the risk of perinatal mortality (OR = 1.06, 95% CI: 0.92-1.22) and GA (OR = 0.10, 95% CI -0.88-1.08). Singleton pregnancy after FET was associated with higher LGA rate (OR = 1.63, 95 %CI: 1.57-1.69) and Macrosomia rate (OR = 1.82, 95% CI: 1.74-1.89). **Conclusion:** Singleton pregnancy after FET have a better perinatal outcome compared with that after fresh ET, except for macrosomia and LGA. The limitations includes the defect of some of the studies included: variation in design, exclusion & inclusion criteria, small number of subjects in some studies and lack of adjustment for important confounders such as age, parity, smoking, duration of infertility. This study is useful to advise patients about the safety in the perinatal results of IVF with FET. **Disclosure of interest:** There is no conflict of interest for any author of this manuscript

P016

ACHIEVED GESTATION RATES AFTER CONJUGAL ARTIFICIAL INSEMINATION DEPENDING ON THE PHYSICIAN'S TECHNIQUE EXPERIENCE

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Objective: Intrauterine conjugal artificial insemination (ICAI) has been used as first-line treatment in infertile couples for 50 years, enhancing a relatively easy-to-perform procedure. Several factors are known to influence ICAI's success: woman's age, infertility evolution, sperm quality, sampling-until-insemination time, etc. The aim of this retrospective cohort study is to analyze whether the physician's technique experience may also affect pregnancy rates after ICAI. **Methods:** 979 infertile patients undergoing ICAI were recruited in Hospital del Mar (Barcelona) Jan2009- Dec2012, including couples with mild male factor, GI-II endometriosis and unilateral tubal factor. Same ovarian stimulation protocols were used among them: recFSH 75-150IU daily from cycle day 3, dosage adjusted on day 5 and every 48h based on observed follicular growth by ultrasound until 18 mm, +Rec-hCG 250ug for final oocyte maturation. ICAI was performed 36hs later by specialist senior physician (709 patients) or junior (270 patients), all with equally-prepared semen and ultrasound-guided. Data collected and checked to be comparable in both groups included age, parity, BMI, infertility time and cause, motile sperm count, antral follicle count, basal-FSH, number of follicles 16mm, serum-FSH and E2 levels on day 3, and follicle number on hCG-day. Main outcome measures after ICAI were: biochemical gestation rate (positive hCG after 3 weeks), pregnancy rate (visible gestational sac by ultrasound at 6 weeks), and at-term pregnancy (delivery 37 weeks); assessed between groups using Pearson Chi-square test. **Results:** From 133/979 diagnosed biochemical pregnancies; 112(84.2%) had been inseminated by senior and 21(15.8%) by junior practitioners. **Biochemical gestation rate was 15.8% for seniors vs. 7.8% for juniors (p=0.001).** Among them 125/979 patients got clinically pregnant; 104(83.2%) from senior ICAI and 21(16.8%) from juniors'. **Pregnancy rate was 14.7% for seniors vs. 7.8% for juniors (p=0.002).** Finally 91/979 cases achieved term pregnancies; 79(86.8%) from senior ICAI and 12(13.2%) from juniors'. **At-term pregnancy rate was 11.2% for seniors vs. 4.4% for juniors (p=0.001).** As secondary findings, no differences either in miscarriage rates or multiple gestation rates were found between groups. **Conclusion:** Practitioners' technique experience seems to affect pregnancy rates resulting from ICAI, which stands out the relevance of its performance learning curve.

P017

A RETROSPECTIVE STUDY ON THE PREVALENCE OF EMPTY FOLLICLE SYNDROME AT A SINGLE FERTILITY CENTER

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Empty follicle syndrome (EFS) is a condition in which no oocytes are retrieved after an apparently adequate ovarian response to stimulation and meticulous follicular aspiration. EFS can be classified into 'genuine' and 'false' types according to hCG levels. It is a rare condition of obscure etiology. The existence of genuine EFS has been questioned and is still controversial. Management of patients with EFS is a challenge to physicians. No single treatment is known to be universally effective. However, patients should be adequately informed regarding the importance of correct hCG administration because improper hCG administration is a common and preventable cause of EFS. EFS is a syndrome that deserves

additional study because such investigation could lead to a further understanding of ovarian biology and infertility. **Objective:** To describe the prevalence of empty follicle syndrome (EFS) at assisted reproductive technology (ART). **Design:** Retrospective study Setting: Large private fertility center. **Patients:** A total of 580 patients who underwent ART between 2003 and 2013 August. Intervention: None. **Main Outcome Measure:** The failure to recover an oocyte during oocyte retrieval at assisted reproductive technology (ART). **Result:** Three cases of EFS were identified in the cohort examined. The prevalence of EFS was 0.52%. **Conclusion:** EFS is a rare occurrence. Because this syndrome tends to recur with dismal pregnancy rates at ART, continued identification and further investigation of the syndrome are needed. Key Words: Empty Follicle Syndrome, follicle maturation, assisted reproduction, oocyte development, follicle development, Infertility, Ovarian stimulation, Retrieval, Oocyte, Chorionic gonadotropin

P018

TRANSCRIPTIONAL ANALYSIS OF GENES ENCODING PROTEINS PRESENTED IN THE EXTRACELLULAR SPACE OF ENDOMETRIAL STROMAL CELLS IN HUMAN

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Problem statement: In *in-vivo* endometrium, endometrial cells experience dramatic alterations during the menstrual cycle by a variety of hormones secreted from sexual organs. These hormonal regulations make it difficult to study physiological and pharmacological aspects of endometrial biology. Therefore, organization of artificial uterine tissues through construction of non-cellular niche mimicking microenvironment enclosing endometrium is important for eliminating chaotic treatment effects detected in the implantation-related studies. Accordingly, as a step towards constructing a precisely defined three dimensional microenvironment engineering extracellular signaling to regulate physiological characteristics of endometrial cells derived from human uterus, information on microenvironment factors presented in the extracellular space of human endometrial stromal cells (hESCs) should be requested. **Methods:** we conducted transcriptional analysis of genes encoding extracellular matrix, cell-to-cell interaction, and integrin proteins expressed in hESCs. Each transcriptional level was measured by real-time polymerase chain reaction (RT-PCR). **Results:** In case of extracellular matrix proteins, 2 (*COL1* and *COLIII*) genes showed significantly higher transcriptional level than the other genes, whereas 7 (*FN*, *NID*, *LN*, *TN*, *ELN*, *COLIV* and *COL V*) genes were weakly transcribed and no transcription of *COLII* and *COLXI* was detected. Moreover, in the cell-to-cell interaction proteins, *CDH2* showed significantly the strongest transcription compared to the other genes and 7 (*CDH1*, *CDH3*, *DSG2*, *ICAM1*, *HSPG2*, *VCAN* and *SDC1*) genes showed extremely low transcriptional level with no transcription of *DSC3*, *PECAM1* and *SELL*. Finally, among total 25 integrin subunit genes, 4 integrin alpha subunit (*ITGA1*, *ITGA3*, *ITGA4* and *ITGAV*) and 3 integrin beta subunit (*ITGB1*, *ITGB3* and *ITGB5*) genes showed significantly increased transcriptional level compared to the other genes, whereas 10 integrin alpha subunit (*ITGA2*, *ITGA5*, *ITGA6*, *ITGA7*, *ITGA8*, *ITGA9*, *ITGA10*, *ITGA11*, *ITGAL* and *ITGAX*) and 3 integrin beta subunit (*ITGB2*, *ITGB4* and *ITGB8*) genes were weakly transcribed with no transcription of *ITGAM*, *ITGAD*, *ITGAE*, *ITGB6* and *ITGB7*. **Conclusion:** we could identify types of extracellular matrix (*COLI* and *COLIII*), cell-to-cell interaction (*CDH2*), and integrin protein (*ITGA1*, *ITGA3*, *ITGA4*, *ITGAV*, *ITGB1*, *ITGB3* and *ITGB5*) -encoding genes significantly up-regulated transcriptionally in hESCs. We have no conflict of interest to declare. Funding: NRF-2017R1A2B4009777



P019

IS BODY MASS INDEX (BMI) AN IMPORTANT PREDICTOR OF ART TREATMENT OUTCOMES? A MALAYSIAN PUBLIC FERTILITY CLINIC EXPERIENCE

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Problem statement: Obesity may place pregnant women at the various obstetrical risks such as gestational diabetes, hypertension and operative delivery. Body mass index (BMI) influences fertility treatment success rate too. This study aimed to investigate influence of BMI on the reproductive outcome of women who had undergone In vitro fertilization (IVF)/Intracytoplasmic sperm injection (ICSI). **Methods:** This retrospective analysis included 108 cycles of women aged younger than 42 years old, undergoing IVF/ICSI and embryos cryopreservation followed by Frozen Embryo Transfer (FET) as part of Segmentation IVF/ICSI treatment commonly practiced at our centre. The FET treatment cycles were divided into four (4) groups according to their BMI: Group 1 Underweight BMI 18.5kg/m², Group 2 Normal 18.5-24.9kg/m², Group 3 Overweight 25-29.9kg/m² and Group 4 Obese ≥30kg/m². Ongoing pregnancy rate (OPR) was measured as primary, whereas biochemical pregnancy rate (bPR), implantation rates (IR) and clinical pregnancy rate (CPR) as secondary end points. Age, types and causes of infertility were analysed. Total dosage of follicle stimulation hormone (FSH) used, number of top quality embryos and number of embryos transferred were recorded. Chi-square analyses were used to determine if BMI has statistically significant difference. **Results:** Background characteristics including age, infertility types and causes in all treatment cycles were similar across the groups except for a significant differences in mean duration of infertility and total dose of FSH used. OPR appeared to be highest in Group 1 at 25% and lowest in Group 3 at 14%. However it was not statistically significant across all BMI groups. Secondary outcomes such as bCPR, IR and CPR in all groups analysed were also not statistically significant. **Conclusion:** Overweight patients were found to have reduced OPR when compared to obese patients. The normal weight patients had similar OPR when compared to obese patients. A larger, well-designed prospective study is needed to further clarify role of BMI in pregnancy outcome of women undergoing ART treatment. This small study showed no statistically significant effect of BMI on embryo quality and subsequently ongoing pregnancy outcome. However, a careful consideration needs to be weighed in view of known obstetrical and maternal complications related to higher BMI.

P020

WEIGHT OF NEWBORNS AFTER TRANSFER OF SINGLE EITHER FRESH OR CRYOPRESERVED EMBRYO IN THE IVF CYCLE

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Problem statement Cryopreservation of embryos is an integral part of assisted reproductive technologies (ART) in the treatment of infertility. Indications for embryo freezing may be in case of risk of hyperstimulation syndrome occurrence in patient in a fresh cycle, embryo preservation for carrying out in further embryo transfers, preimplantation genetic screening or in the case of "freeze-all" policy of ART clinic. The weight of newborns, the duration of the histatio period, the rate of delivery by Caesarean section are important indicators for evaluating the outcomes of embryo transfer. In this regards it is important to study these parameters after transfer of cryopreserved embryo. **Methods** The obstetric and

perinatal outcomes of 155 pregnancies of patients undergoing infertility treatment with ART methods in 2015-2016 at the Clinic of Reproductive Medicine "Nadiya" were retrospectively analyzed. Group 1 (n=35) were patients with transfer of single fresh embryo, group 2 (n=62) – with a transfer of single cryopreserved embryo, group 3 (n=58) – pregnancy occurred spontaneously. **Results** The body mass index of the patients in the studied groups was comparable. The survival rate of embryos after cryopreservation was 96%, and the pregnancy rate in group 2 was 49.3%. The percentage of preterm delivery in groups 1 to 3 was 6.45, 14.2 and 8.6%, respectively. The rate of delivery by Cesarean section in groups 1 to 3 was 61.3, 34.2 and 32.7%, respectively. Appgar scores of newborns have no significant differences in all study groups. The gestation period corresponded (37.6 ± 1.2), (38.8 ± 2.2) and (39.3 ± 2.1) weeks for groups 1-3, respectively. The weight of children at birth in these groups was (3,653.3 ± 550.5), (3,087 ± 704.7) and (3,420.2 ± 547.1) g, height made (53.6 ± 3.3), (50.6 ± 5.0) and (52.1 ± 3.0) g, respectively. Perinatal losses, birth injuries, malformations in children of all the studied groups were not revealed. **Conclusion** Delivery by Cesarean section is performed more often and the birth weight of the newborn is significantly higher after cryopreserved embryo transfer. Cryopreservation factors do not increase adversely affect the physical health of children.

P021

PREGNANCY OUTCOMES OF PATIENTS ACCORDING TO AGE WITH EXTREMELY LOW SERUM ANTI-MÜLLERIAN HORMONE IN IVF-ET CYCLES

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Problem statement: Anti-Müllerian hormone (AMH) as a tool to predict ovarian responsiveness to controlled ovarian hyperstimulation (COH) has been used currently. Despite a strong positive correlation between serum AMH level and ovarian response to COH, the role of serum AMH as a tool to predict clinical outcomes is a matter of debate. Especially in young women with extremely low serum AMH is more pronounced debate. Therefore, the aim of this study was to compare the IVF outcomes according to age in women with extremely low serum AMH. **Methods:** The outcome of 344 fresh IVF cycles in 199 patients with serum AMH level between 0.1 and 0.2ng/ml was retrospectively analyzed, observed from January 2014 to December 2016 in single infertility center. From the database, cycle cancellation rate, implantation rate (IR), clinical pregnancy rate (CPR), live birth rate (LBR) were compared between the group in three age groups. The first group was from 30 to 34 years old. The age of second group was from 35 to 39. The third group was from 40 to 43 years old. **Results:** There were no significant differences in cycle cancellation rate between three groups (17.3% vs. 15.3% vs. 21.8%, p0.05). Also, the number of mature oocytes and fertilization rate were no significant differences. Among those who reached oocyte pick up (OPU), age significantly affected the success rate: patients under 40 years had significantly better implantation rate (IR: Group 1 22.2% vs. Group 3 3.5%, Group 2 14.3% vs. Group 3 3.5%, p0.05), clinical pregnancy rate (CPR: Group1 29.2% vs. Group 3 8.9%, p0.05), and live birth rate (LBR: Group 1 25.0% vs. Group 3 2.2%, Group 2 13.0% vs. Group 3 2.2%, p0.05) than patients aged 40-43. **Conclusion:** Under 40 years old had significantly better IR, CPR and LBR than group of over 40 years age. Therefore, patients under 40 years of age with extremely low serum AMH levels may be consider IVF procedure and still have chances of achieving a pregnancy. We also may provide appropriate counseling and information.



P022

PREDICTORS OF HUMAN BLASTOCYST HATCHING SUCCESS IN ASSISTED REPRODUCTION

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Problem statement. Molecular mechanisms of hatching have still not been completely studied. The aim of the study was to identify genetic predictors of human blastocyst hatching success in assisted reproduction. **Methods** The study included 83 blastocysts. The hatching group included 36 blastocysts (43.4%), which underwent spontaneous hatching. The control group included 47 blastocysts (56.6%) that did not undergo spontaneous hatching. Hatching success assessment was performed after 144–146 hours post fertilization. The mRNA expression levels of cathepsin V (CTSV), GATA binding protein 3 (GATA3) and human chorionic gonadotropin beta (CGB) genes were detected by quantitative polymerase chain reaction. **Results** The rate of blastocysts with the **thickening of the ZP** was similar in the groups (11.1% vs 17.0%). The rate of blastocysts of the 5th stage of development was significantly higher in the hatching group, and blastocysts of the 2nd and 3rd stage of development were detected only in the control group. In 63.8% of cases, **inner cell mass (ICM)** was evaluated as grade A (28.9%) and B (34.9%). In an equal number of cases, **trophectoderm (TE)** was evaluated as grade A (33.7%), B (36.2%) and C (30.1%). Grade A TE was detected in 47.2% of embryos in the hatching group but only in 23.4% of embryos in the control group. Grade C TE was detected in 44.7% of control blastocysts and only in 11.1% in the hatching blastocysts ($p = 0.0030$). The blastocysts in the control group had lower expression for the CTSV (3.9 vs 4.4, $p=0.0001$), GATA3 (4.5 vs 4.7, $p=0.0005$) and CGB (1.3 vs 2.1, $p=0.0004$) genes. **Conclusion** We did not find an association between the rate of hatching failure and ZP thickness. The high blastocysts quality of Gardner scale parameters had a positive effect on hatching success. The expression of CGB, CTSV and GATA3 genes was higher in the hatching group. The efficacy of spontaneous hatching is not determined by the quality of the ZP, but by the quality of the blastocysts themselves. The authors report no conflicts of interest.

P023

COMPARISON OF CLINICAL OUTCOMES OF FRESH AND FROZEN EMBRYO TRANSFERS AFTER MORPHOLOGY-BASED EMBRYO SELECTION

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Problem statement: Recent improvement of vitrification technologies allows us to choose between fresh and frozen embryo transfer (ET) procedure. Some studies have suggested that frozen ET cycles may provide clinical advantages in case of all patients. However, others have concluded that frozen ET is beneficial only in selected patient population. This study aimed to compare the outcome of the *in vitro* fertilization cycles of fresh versus frozen ET, when the selection of embryos for transfer was based on the morphology of available blastocysts. **Methods:** In this retrospective study, we analysed 672 ET cycles performed at our infertility clinic between January 2013 and December 2017. All embryos were fertilised by intracytoplasmic sperm injection and transferred at blastocyst stage (day 5 or 6) after morphology-based selection. The measured outcomes were implantation rate, clinical pregnancy rate, miscarriage rate and ongoing pregnancy rate. **Results:** Data from 263 fresh and 409 frozen ET cycles were analysed. The average female age was similar in both groups (37,35 ± 5,17 in the fresh ET group and 36,79 ± 5,03 in the frozen

ET group). The study groups also did not vary in the average number of embryos transferred per cycle (1,31 ± 0,51 and 1,30 ± 0,49). No significant difference was found in any of the outcomes measured. The implantation rate was similar in the two groups, 31,99% after fresh ET cycles and 31,20% after frozen ET cycles ($p=0,8064$). The clinical pregnancy rate was slightly higher in the fresh ET group (34,22%) compared to the frozen ET group (30,56%), however, the difference was not significant ($p=0,3211$). The miscarriage rates also did not differ significantly (23,42% and 27,11%, respectively; $p=0,4912$). Fresh ET cycles resulted in higher ongoing pregnancy rate than frozen ET cycles, but not significantly (26,24% compared to 23,23%; $p=0,3755$). **Conclusion:** In contrast to previous studies, we found that clinical outcomes do not differ significantly between fresh and frozen ET cycles when the embryo selection is based on morphological criteria. Therefore, the optimal strategy for ET can be selected according to individual needs and circumstances of the patients.

P024

OPTIMIZATION OF IVF PROTOCOLS IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

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Problem statement: The main principal problem in Polycystic ovarian syndrome (PCOS) patients undergoing IVF were poor oocyte quality, low fertilization rates, and high miscarriage rates. Although various protocols have been used, the clinical outcomes of PCOS patients remain unsatisfactory. We assumed, that Clomiphene citrate 50 mg/d can demonstrated to be an effective oral alternative for preventing premature LH surges during controlled ovarian hyperstimulation (COH) in PCOS women undergoing IVF/ICSI treatments, with optimal pregnant outcomes in frozen-thawed embryo transfer cycles. **Methods:** The Clomiphene citrate 50 mg/d from MC2 was administered until the trigger day in 62 PCOS patients enrolled in the study group. Human menopausal gonadotropin (hMG) 150 to 225IU from MC7 till the trigger day. The final stage of oocyte maturation was triggered using triptorelin 0.2mg. A short protocol was used for 38 PCOS women in the control group. Patients were administered 0.1mg of triptorelin daily beginning on MC2 and 150 to 225IU of hMG daily beginning on MC3. HCG 3000 IU was injected when dominant follicles reached 18mm in diameter. **Results:** The primary outcome was the viable embryo rate per oocyte retrieved. The secondary outcomes included the number of oocytes retrieved, fertilization rate, and clinical pregnancy outcomes from FET cycles. No significant between-group differences were observed in the number of oocytes retrieved (13.1±7.76 vs 12.9±7.88), number of viable embryos (5.31±3.17 vs 4.9±3.32), mature oocyte rate (90.31±10.01% vs 92.8±9.21%), and cleavage rate (96.88±5.92% vs 94.91±8.97%). The fertilization rate (75.91±18.87% vs 68.73±20.71%; $P<0.05$), viable embryo rate per oocyte retrieved (39.84% vs 34.67%; $P<0.05$), biochemical pregnancy rate (71.43% vs 55.56%; $P<0.05$), clinical pregnancy rate (65.31% vs 48.89%; $P<0.05$), and implantation rate (46.47% vs 31.18%; $P<0.05$) in the study group were significant higher than those in the control group. This study shows that new protocol was feasible to improve the oocyte quality, possibly providing a new choice for PCOS patients undergoing IVF/ICSI treatments in combination with embryo cryopreservation. **Conclusion:** This novel protocol is promising with the advantages of cost reduction, being well tolerated, user convenience, which will help to establish a convenient user regimen in combination with a "freeze all" strategy.



P025

THE INFLUENCE OF MERCURY, MANGANESE, MOLYBDENUM AND NICKEL CONCENTRATIONS IN FOLLICULAR FLUID ON EMBRYO DEVELOPMENTAL DYNAMICS

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Problem statement: The negative impact of the environment in which the egg cell grows affects the quality of the embryo and the time at which subsequent developmental stages are reached which ultimately translates into achievement of pregnancy. One suggested cause of egg-cell damage is the deleterious effects of excess amounts of heavy metals. **Methods:** This study involved 252 women aged 25–35 years undergoing fresh IVF in 2017. The growth of all the embryos from each patient was monitored continuously. The mercury (Hg), manganese (Mn), molybdenum (Mo) and nickel (Ni) measurements were performed by the electrothermal-atomic absorption spectrometry method in follicular fluid. Clinical pregnancy was confirmed with a TVUSG examination for the presence of gestational sac and live embryo in the uterine cavity. The aim of this research was to specify the influence of Hg, Mn, Mo and Ni on the dynamics of embryo development. **Results:** It has been shown that the concentrations of Hg in the follicular fluid affect the dynamics of embryo development from the last observation of both pronuclei (tC) to the eight-cell stage embryo(t8). The concentration of Mn, Mo and Ni does not have an impact on the dynamics of embryo development. In order to determine whether the fact of obtaining pregnancy is affected by the variables, a logistic regression model was employed. The dependent variable was the fact of achieving pregnancy, and the independent variable was the level of the trace metals. Ultimately, only one variable remained statistically significant in the model: the level of Hg. **Conclusion:** Exposure to Mercury in the reproductive period impacts the dynamics of embryo development and achieving pregnancy in fresh IVF. Authors declare no conflict of interest.

P026

IS STIMULATION DAY 6 (S6) ESTRADIOL A PREDICTOR OF TREATMENT OUTCOMES IN IVF/ICSI CYCLES? A MALAYSIAN PUBLIC FERTILITY CLINIC EXPERIENCE

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Problem statement: The success of In vitro fertilization (IVF)/Intracytoplasmic sperm injection (ICSI) depends on controlled ovarian hyperstimulation (COH) resulting in multi-follicular response. Serum estradiol (E2) plays an important role in oocytes/follicular maturation. This study aimed to assess the role of S6 E2 COH in IVF/ICSI cycle outcomes. **Methods:** This retrospective analysis included 129 cycles of women aged younger than 42 years old, undergoing IVF/ICSI at our centre. The treatment cycles were divided into three (3) groups according to their S6 E2 levels: Group I 1500nmol/mL, Group II 1500-3500nmol/mL and Group III 3500nmol/mL. Embryo usage rates (EUR) were measured as primary endpoint. Proportion of usable MII oocytes retrieved during ovum pick up (OPU), fertilization rates and proportion of top quality embryos (TQE) were analysed at secondary endpoints. Serum E2 on day 2 (D2) and ovulation trigger day (OTD) were compared. Age, Body Mass Index (BMI), duration of COH, total FSH dosage, duration, types and causes of infertility were recorded. Data were analysed using chi-square and ANOVA. **Results:** Background characteristics including age, BMI, infertility causes and total FSH were comparable except for a significant difference in mean duration of infertility and duration of COH across all groups. EUR was lowest in Group III at 79.3% and highest in

Group II at 85.4% but it was not statistically significant. There were no significant differences in fertilisation rate, number of TQE, D2 E2 and OTD E2 between all groups compared. There was an inverse association between D2 E2 but a positive correlation with OTD E2 across all three groups. There was a significantly higher number of oocytes collected at 15.1 and available MII oocytes in Group III at 13.4. **Conclusion:** Higher S6 E2 during ovarian stimulation leads higher E2 on OTD. This translates to a significantly more oocytes collected and top quality embryos produced. However there is a reduction in fertilisation and embryo usage rates as estradiol level increases. Risk of ovarian hyperstimulation syndrome is clinically significant at higher E2 level. A larger, well-designed prospective study is needed to further clarify role estradiol level in predicting outcome of women undergoing ART treatment including pregnancy rates.

P027

THE EFFECT OF LATERALITY OF ENDOMETRIOMA IN IVF/ICSI CYCLES

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Problem Statement: Endometriosis, the most common gynecological disorder, is a challenging disease observed in 20%-40% of subfertile women. Endometriomas affect 17-44% of women with endometriosis. Because endometrioma has detrimental effects on fertility, many of these women need Assisted Reproductive Technology (ART) to conceive. In this study, we aimed to investigate the effects of endometrioma presence and laterality over In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) outcomes. **Methods:** The study was designed retrospectively. A total of 159 women enrolled in IVF / ICSI cycles between March 2015-March 2018, were included. Patients were divided into two groups as Endometrioma group (n: 73) and control group (n:86). In Endometrioma group, subgroup analysis was performed according to laterality. Demographic characters, clinical and laboratory parameters were recorded. SPSS was used for analysis. **Results:** There were no significant differences between groups with respect to age, BMI, stimulation protocols. In endometrioma group, although basal FSH levels was higher than control group, it was within normal limits, while estradiol levels was lower (p0.001, p 0.042, respectively). Antral Follicle count (AFC), dominant follicle number, total oocyte count, MII oocyte numbers were found to be significantly lower, whereas numbers of embryos achieved, clinical pregnancy rates were found to be similar. In endometrioma group, there were 4 patients with no dominant follicle development and 8 total fertilization failures were observed. With respect to laterality, there were no statistically significant differences in terms of Antimullerian Hormone (AMH) levels, oocyte and embryo quality, the numbers of embryos achieved, pregnancy rates between two groups. When compared according to previous history of surgery (26 patients), AFC and AMH levels were found to be lower in patients who underwent surgery, while there was no significant difference regarding oocyte numbers, embryo quality and pregnancy rates. **Conclusion:** This study shows that presence of endometrioma negatively affects on fertility parameters like FSH levels, AFC and MII oocyte numbers, albeit no significant effect over embryo quality and pregnancy rates whereas laterality of endometrioma doesn't have any influence over any fertility parameters and pregnancy rates.

	Substratum			P
	Group	Control	Intervention	
Age	32.1 (2.1)	32.0 (2.1)	32.1 (2.1)	0.889
Sex	23.3 (1.1)	23.3 (1.1)	23.3 (1.1)	0.889
Year	4 (2.1)	4 (2.1)	4 (2.1)	0.889
Year 10	1.4 (0.1)	1.4 (0.1)	1.4 (0.1)	0.779
Year 20	2.8 (0.1)	2.8 (0.1)	2.8 (0.1)	0.889
Year 30	5.6 (0.1)	5.6 (0.1)	5.6 (0.1)	0.889
Year 40	11.2 (0.1)	11.2 (0.1)	11.2 (0.1)	0.889
Year 50	22.4 (0.1)	22.4 (0.1)	22.4 (0.1)	0.889
Year 60	44.8 (0.1)	44.8 (0.1)	44.8 (0.1)	0.889
Year 70	89.6 (0.1)	89.6 (0.1)	89.6 (0.1)	0.889
Year 80	179.2 (0.1)	179.2 (0.1)	179.2 (0.1)	0.889
Year 90	358.4 (0.1)	358.4 (0.1)	358.4 (0.1)	0.889
Year 100	716.8 (0.1)	716.8 (0.1)	716.8 (0.1)	0.889
Year 110	1433.6 (0.1)	1433.6 (0.1)	1433.6 (0.1)	0.889
Year 120	2867.2 (0.1)	2867.2 (0.1)	2867.2 (0.1)	0.889
Year 130	5734.4 (0.1)	5734.4 (0.1)	5734.4 (0.1)	0.889
Year 140	11468.8 (0.1)	11468.8 (0.1)	11468.8 (0.1)	0.889
Year 150	22937.6 (0.1)	22937.6 (0.1)	22937.6 (0.1)	0.889
Year 160	45875.2 (0.1)	45875.2 (0.1)	45875.2 (0.1)	0.889
Year 170	91750.4 (0.1)	91750.4 (0.1)	91750.4 (0.1)	0.889
Year 180	183500.8 (0.1)	183500.8 (0.1)	183500.8 (0.1)	0.889
Year 190	367001.6 (0.1)	367001.6 (0.1)	367001.6 (0.1)	0.889
Year 200	734003.2 (0.1)	734003.2 (0.1)	734003.2 (0.1)	0.889
Year 210	1468006.4 (0.1)	1468006.4 (0.1)	1468006.4 (0.1)	0.889
Year 220	2936012.8 (0.1)	2936012.8 (0.1)	2936012.8 (0.1)	0.889
Year 230	5872025.6 (0.1)	5872025.6 (0.1)	5872025.6 (0.1)	0.889
Year 240	11744051.2 (0.1)	11744051.2 (0.1)	11744051.2 (0.1)	0.889
Year 250	23488102.4 (0.1)	23488102.4 (0.1)	23488102.4 (0.1)	0.889
Year 260	46976204.8 (0.1)	46976204.8 (0.1)	46976204.8 (0.1)	0.889
Year 270	93952409.6 (0.1)	93952409.6 (0.1)	93952409.6 (0.1)	0.889
Year 280	187904819.2 (0.1)	187904819.2 (0.1)	187904819.2 (0.1)	0.889
Year 290	375809638.4 (0.1)	375809638.4 (0.1)	375809638.4 (0.1)	0.889
Year 300	751619276.8 (0.1)	751619276.8 (0.1)	751619276.8 (0.1)	0.889
Year 310	1503238553.6 (0.1)	1503238553.6 (0.1)	1503238553.6 (0.1)	0.889
Year 320	3006477107.2 (0.1)	3006477107.2 (0.1)	3006477107.2 (0.1)	0.889
Year 330	6012954214.4 (0.1)	6012954214.4 (0.1)	6012954214.4 (0.1)	0.889
Year 340	12025908428.8 (0.1)	12025908428.8 (0.1)	12025908428.8 (0.1)	0.889
Year 350	24051816857.6 (0.1)	24051816857.6 (0.1)	24051816857.6 (0.1)	0.889
Year 360	48103633715.2 (0.1)	48103633715.2 (0.1)	48103633715.2 (0.1)	0.889
Year 370	96207267430.4 (0.1)	96207267430.4 (0.1)	96207267430.4 (0.1)	0.889
Year 380	192414534860.8 (0.1)	192414534860.8 (0.1)	192414534860.8 (0.1)	0.889
Year 390	384829069721.6 (0.1)	384829069721.6 (0.1)	384829069721.6 (0.1)	0.889
Year 400	769658139443.2 (0.1)	769658139443.2 (0.1)	769658139443.2 (0.1)	0.889
Year 410	1539316278886.4 (0.1)	1539316278886.4 (0.1)	1539316278886.4 (0.1)	0.889
Year 420	3078632557772.8 (0.1)	3078632557772.8 (0.1)	3078632557772.8 (0.1)	0.889
Year 430	6157265115545.6 (0.1)	6157265115545.6 (0.1)	6157265115545.6 (0.1)	0.889
Year 440	12314530231091.2 (0.1)	12314530231091.2 (0.1)	12314530231091.2 (0.1)	0.889
Year 450	24629060462182.4 (0.1)	24629060462182.4 (0.1)	24629060462182.4 (0.1)	0.889
Year 460	49258120924364.8 (0.1)	49258120924364.8 (0.1)	49258120924364.8 (0.1)	0.889
Year 470	98516241848729.6 (0.1)	98516241848729.6 (0.1)	98516241848729.6 (0.1)	0.889
Year 480	197032483697459.2 (0.1)	197032483697459.2 (0.1)	197032483697459.2 (0.1)	0.889
Year 490	394064967394918.4 (0.1)	394064967394918.4 (0.1)	394064967394918.4 (0.1)	0.889
Year 500	788129934789836.8 (0.1)	788129934789836.8 (0.1)	788129934789836.8 (0.1)	0.889
Year 510	1576259869579673.6 (0.1)	1576259869579673.6 (0.1)	1576259869579673.6 (0.1)	0.889
Year 520	3152519739159347.2 (0.1)	3152519739159347.2 (0.1)	3152519739159347.2 (0.1)	0.889
Year 530	6305039478318694.4 (0.1)	6305039478318694.4 (0.1)	6305039478318694.4 (0.1)	0.889
Year 540	12610078956637388.8 (0.1)	12610078956637388.8 (0.1)	12610078956637388.8 (0.1)	0.889
Year 550	25220157913274777.6 (0.1)	25220157913274777.6 (0.1)	25220157913274777.6 (0.1)	0.889
Year 560	50440315826549555.2 (0.1)	50440315826549555.2 (0.1)	50440315826549555.2 (0.1)	0.889
Year 570	100880637653099110.4 (0.1)	100880637653099110.4 (0.1)	100880637653099110.4 (0.1)	0.889
Year 580	201761275306198220.8 (0.1)	201761275306198220.8 (0.1)	201761275306198220.8 (0.1)	0.889
Year 590	403522550612396441.6 (0.1)	403522550612396441.6 (0.1)	403522550612396441.6 (0.1)	0.889
Year 600	807045101224792883.2 (0.1)	807045101224792883.2 (0.1)	807045101224792883.2 (0.1)	0.889
Year 610	1614090202449585766.4 (0.1)	1614090202449585766.4 (0.1)	1614090202449585766.4 (0.1)	0.889
Year 620	3228180404899171532.8 (0.1)	3228180404899171532.8 (0.1)	3228180404899171532.8 (0.1)	0.889
Year 630	6456360809798343065.6 (0.1)	6456360809798343065.6 (0.1)	6456360809798343065.6 (0.1)	0.889
Year 640	12912721619596686131.2 (0.1)	12912721619596686131.2 (0.1)	12912721619596686131.2 (0.1)	0.889
Year 650	25825443239193372262.4 (0.1)	25825443239193372262.4 (0.1)	25825443239193372262.4 (0.1)	0.889
Year 660	51650886478386744524.8 (0.1)	51650886478386744524.8 (0.1)	51650886478386744524.8 (0.1)	0.889
Year 670	103301772956773489049.6 (0.1)	103301772956773489049.6 (0.1)	103301772956773489049.6 (0.1)	0.889
Year 680	206603545913546978099.2 (0.1)	206603545913546978099.2 (0.1)	206603545913546978099.2 (0.1)	0.889
Year 690	413207091827093956198.4 (0.1)	413207091827093956198.4 (0.1)	413207091827093956198.4 (0.1)	0.889
Year 700	826414183654187912396.8 (0.1)	826414183654187912396.8 (0.1)	826414183654187912396.8 (0.1)	0.889
Year 710	1652828367308375824793.6 (0.1)	1652828367308375824793.6 (0.1)	1652828367308375824793.6 (0.1)	0.889
Year 720	3305656734616751649587.2 (0.1)	3305656734616751649587.2 (0.1)	3305656734616751649587.2 (0.1)	0.889
Year 730	6611313469233503299174.4 (0.1)	6611313469233503299174.4 (0.1)	6611313469233503299174.4 (0.1)	0.889
Year 740	13222626938467006598348.8 (0.1)	13222626938467006598348.8 (0.1)	13222626938467006598348.8 (0.1)	0.889
Year 750	26445253876934013196697.6 (0.1)	26445253876934013196697.6 (0.1)	26445253876934013196697.6 (0.1)	0.889
Year 760	52890507753868026393395.2 (0.1)	52890507753868026393395.2 (0.1)	52890507753868026393395.2 (0.1)	0.889
Year 770	105781015507736052786790.4 (0.1)	105781015507736052786790.4 (0.1)	105781015507736052786790.4 (0.1)	0.889
Year 780	211562031015472105573580.8 (0.1)	211562031015472105573580.8 (0.1)	211562031015472105573580.8 (0.1)	0.889
Year 790	4231240620309442111471616 (0.1)	4231240620309442111471616 (0.1)	4231240620309442111471616 (0.1)	0.889
Year 800	8462481240618884222943232 (0.1)	8462481240618884222943232 (0.1)	8462481240618884222943232 (0.1)	0.889
Year 810	16924962481237768768486464 (0.1)	16924962481237768768486464 (0.1)	16924962481237768768486464 (0.1)	0.889
Year 820	33849924962475537536972928 (0.1)	33849924962475537536972928 (0.1)	33849924962475537536972928 (0.1)	0.889
Year 830	67699849924951075073945856 (0.1)	67699849924951075073945856 (0.1)	67699849924951075073945856 (0.1)	0.889
Year 840	135399699849102150147891712 (0.1)	135399699849102150147891712 (0.1)	135399699849102150147891712 (0.1)	0.889
Year 850	270799399698204300295783424 (0.1)	270799399698204300295783424 (0.1)	270799399698204300295783424 (0.1)	0.889
Year 860	541598799396408600591566848 (0.1)	541598799396408600591566848 (0.1)	541598799396408600591566848 (0.1)	0.889
Year 870	1083197598792817201183133696 (0.1)	1083197598792817201183133696 (0.1)	1083197598792817201183133696 (0.1)	0.889
Year 880	2166395197585634402366267392 (0.1)	2166395197585634402366267392 (0.1)	2166395197585634402366267392 (0.1)	0.889
Year 890	4332790395171268804732534784 (0.1)	4332790395171268804732534784 (0.1)	4332790395171268804732534784 (0.1)	0.889
Year 900	8665580790342537609465069568 (0.1)	8665580790342537609465069568 (0.1)	8665580790342537609465069568 (0.1)	0.889
Year 910	17331161580685075218930139136 (0.1)	17331161580685075218930139136 (0.1)	17331161580685075218930139136 (0.1)	0.889
Year 920	34662323161370150437860278272 (0.1)	34662323161370150437860278272 (0.1)	34662323161370150437860278272 (0.1)	0.889
Year 930	69324646322740300875720556544 (0.1)	69324646322740300875720556544 (0.1)	69324646322740300875720556544 (0.1)	0.889
Year 940	138649292645480601751441113088 (0.1)	138649292645480601751441113088 (0.1)	138649292645480601751441113088 (0.1)	0.889
Year 950	277298585290961203502882226176 (0.1)	277298585290961203502882226176 (0.1)	277298585290961203502882226176 (0.1)	0.889
Year 960	554597170581922407005764452352 (0.1)	554597170581922407005764452352 (0.1)	554597170581922407005764452352 (0.1)	0.889
Year 970	1109194341163844814011528904704 (0.1)	1109194341163844814011528904704 (0.1)	1109194341163844814011528904704 (0.1)	0.889
Year 980	2218388682327689628023057809408 (0.1)	2218388682327689628023057809408 (0.1)	2218388682327689628023057809408 (0.1)	0.889
Year 990	4436777364655379256046115618816 (0.1)	4436777364655379256046115618816 (0.1)	4436777364655379256046115618816 (0.1)	0.889
Year 1000	8873554729310758512092231237632 (0.1)	8873554729310758512092231237632 (0.1)	8873554729310758512092231237632 (0.1)	0.889

Table 1. Baseline characteristics of the study population. Values are mean (SD) or n (%). *Significant compared to non-randomized group. †Significant compared to control group. ‡Significant compared to both groups.

P028
EFFICACY OF LOW MOLECULAR WEIGHT HEPARIN (LMWH) IN RECURRENT REPRODUCTIVE FAILURE WOMEN WITH HIGH VALUE OF PERIPHERAL BLOOD NK CELL PROPORTION

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Problem statement: Peripheral blood NK (pbNK) cell has been associated with reproductive immunopathology such as recurrent pregnancy loss (RPL), recurrent implantation failures (RIF). It was widely accepted that intravenous immunoglobulin G (IVIG) therapy have an effective role in treatment of RPL patients with elevated pbNK cell proportion. On the other hands, the efficacy of LMWH therapy was controversial until nowadays. This study is performed to evaluate the efficacy of LMWH in women with high pbNK cell proportion. **Methods:** Retrospective chart review including 128 patients who suffered from RPL or RIF with high pbNK cell proportion (pbNK cell 12.0%) observed from 2012 to 2016 in single infertility center. The IVIG treatment group was 74 patients and the LMWH treatment group was 54 patients. The role of IVIG was 400mg/kg intravenous injection from oocyte retrieved day or embryo transfer (ET) day to gestational age (GA) 20 weeks at 4 week intervals. The role of LMWH was 40mg to 80mg daily subcutaneously injection from ET day until GA 12 weeks. We analyzed clinical pregnancy rate (CPR), implantation rate (IR), live birth rate (LBR). **Results:** The general characteristics were not different respectively. RPL was higher in LMWH group than IVIG group (41.7% vs. 67.6%, p0.05) and RIF was higher in IVIG group than LMWH group (82.4% vs. 62.2%, p0.05). Despite the difference in indications, IR (31.47% vs. 35.47%), CPR (70.6% vs. 74.4%) and LBR (60.3% vs. 66.7%) were similar between IVIG and LMWH treatment group in fresh cycles. In frozen thawed cycles, IR (31.58% vs. 38.80%), CPR (70.0% vs. 80.0%) and LBR (62.5% vs. 68.6%) were not significantly different between IVIG and LMWH treatment group. According to level of pbNK cell proportion, pregnancy outcomes in LMWH were compatible with IVIG treatment. **Conclusion:** The efficacy of LMWH in recurrent

reproductive failure including RPL and RIF with high value of pbNK cell proportion is compatible IVIG. LMWH plays a role as an immune-modulator in recurrent reproductive failure patients with high value of pbNK cell proportion comparable to that of IVIG.

P030

LIMITS FOR OFFICE HYSTEROSCOPY WITHOUT ANAESTHESIA: PAIN

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Introduction: Office hysteroscopy is a minimally invasive procedure that allows to perform many operative procedures in an ambulatory setting without the need of anaesthesia. **Problem Statement:** To describe the limits of office hysteroscopic procedure and define the pain as the possible main one. **Study Design:** We include the patients that underwent office-based hysteroscopic procedure from September 2017 to June 2018 in our hospital area in Barcelona. It has been performed with a 4 mm office hysteroscope (Bettocchi size 4, Karl Storz). Polyp removal was performed with scissors and teeth forceps, myoma and septum resection were performed with the same instruments and high-power 980 nm diode laser (BioLitec). The office procedure was carried out without any kind of anesthesia, speculum, or Pozzi tenaculum. Patients were prepared with desogestrel for 4 weeks before the procedure to achieve endometrial atrophy. Intravaginal misoprostol 200 µg was indicated the night before. All patients received oral diazepam and ibuprofen, 30 minutes before the procedure. **Results:** A total of 341 women were included. The mean age was 46 years (range of 31-70). 190 polyps, 44 myomas and 11 uterine septum were removed. A total of 84 endometrial biopsies were performed. There were no complications. It was well tolerated in 89% of the cases. 29 patients (11%) reported moderate pain, so the procedure has to be suspended and they were referred to surgery room to complete it under anesthesia. Of these patients, the median time was 6.4 min (range 3-17), 35% were under menopausal status and 4 (13%) did not have sexual intercourse. 75% (22 patients) did not have previous vaginal deliveries, 18 of them were nulipara, while 4 patients had previous cesarean section. Regression analysis was performed to correlate the time, age, parity, menopause state or pathology with the possibility of perform all the procedure at the office state, and there were no differences. **Conclusions:** Office-based hysteroscopic procedures are generally well tolerated. In our center we had an acceptable rate of patients who did not tolerate the procedure for reasons related with the pain, which seems to be the main limit. We didn't find any difference

miscarriage (n=12) had a normoreceptor endometrial response with normal endometrial secretory transformation; H-score of estrogen (ER) and progesterone (PR) receptors in the endometrium were comparable (p0.01), respectively: ER in the glands – 72,2±13,6 and 116,7±11,7; in the stroma – 88,9±12,9 and 145,0±20,1; PR in the glands – 34,4±11,2 and 59,2±17,2; in the stroma – 210,0±17,0 and 260,8±8,0. In 64% women with anamnesis of miscarriage (n=21) morphological characteristics of insufficient secretory phase of the endometrial cycle were revealed. H-score indicators in these women significantly differed from healthy women (p0.01): ER in the glands – 201,9±19,4; in the stroma – 159,0±21,5; PR in the glands – 228,6±15,5; in the stroma – 256,7±7,8. All women had an ovulatory menstrual cycle (m.c.). The E₂, P content in the blood (6-8 days after ovulation), M-echo thickness (12-14 days m.c.) did not differ in the groups. **Conclusion(s).** Almost two thirds of the women with anamnesis of miscarriage in the observed cohort had a decreased endometrial receptivity status.

P032

DENGUE AND MALARIA INFECTION IN PREGNANCY: MATERNAL, FETAL AND NEONATAL OUTCOMES IN A TERTIARY CARE HOSPITAL

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Problem Statement: Malaria and dengue infections are a cause of significant morbidity and mortality. Pregnant women are more susceptible to severe forms of these infections, with poorer outcomes. Our paper aims to study the maternal, fetal, and neonatal outcomes in pregnant patients infected with either dengue or malaria admitted to a tertiary care hospital in Pakistan, a country where malaria and dengue is endemic and on the rise. **Methods:** An observational, retrospective review of patient medical records was carried out for pregnant and post-partum women who were admitted with either dengue or malaria infections from January 2011 to December 2015 inclusive at the Aga Khan University Hospital, in Karachi, Pakistan. Outcomes were compared between these two groups as well as a third group consisting of women diagnosed with multiple infections in addition to dengue and/or malaria as per predefined criteria. **Results:** We included 85 women who were admitted with dengue and/or malaria infections. More women had contracted dengue fever as compared to malaria (56% vs 21%), and 22% of patients were found to have multiple infections. No significant difference in the mean gestational age at delivery was noted among dengue and malaria patients, however a significant difference was seen when compared to the multiple infections group (p0.01), delivering preterm at 30 weeks. The mean neonatal birth weight in malaria patients was significant lower (p=0.02) compared to dengue patients. No significant differences were seen in type of delivery, status of neonate at birth, birth anomalies and birth injuries among the groups. Six women (7%) died during admission due to multi-organ involvement. **Conclusion:** Dengue and malaria remain an under-reported cause of maternal morbidity and mortality. Due to their similar presentation, it is imperative to develop more efficient guidelines to screen and diagnose these infections in pregnancy. **[Keywords:** Dengue, malaria, pregnancy, OBGYN, maternal outcomes, neonatal outcomes]

FETOMATERNAL MEDICINE

P031

ENDOMETRIAL RECEPTIVITY IN WOMEN WITH EARLY MISCARRIAGES IN ANAMNESIS

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Problem statement: Reduced endometrial receptivity may be the cause of early pregnancy loss. **Objective.** To study the receptivity characteristics of the endometrium in women with early miscarriages in the anamnesis. **Methods.** Ultrasound, hormonal examinations, morphological examination of endometrial biopsy specimens were performed. **Participant(s).** 48 women 23-40 years old (mean age 30.3±0.4) were examined: 33 women with early miscarriages in anamnesis (of these 39% (n=13) with recurrent miscarriage); 15 healthy fertile women. All women had a normal level of thyroid hormones, prolactin, androgens in the blood. **Result(s).** Healthy women and 36% patients with anamnesis of

P033

PREVALENCE OF HIGHLY THROMBOGENIC STATE IN PREGNANT PATIENTS WITH INHERITED THROMBOPHILIA

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Problem statement: Inherited thrombophilia represents a coagulation disorder that predispose individuals to thromboembolic events and when associated with pregnancy, it becomes a major risk factor for thromboembolism during pregnancy and in the postpartum period and increases the risk of an adverse pregnancy outcome. **Methods:** We analyzed 455 patients, pregnant at the moment of examination, with ages between 16 and 49 years, recruited over a period of 6 months, from November 2015 to April 2016, in the Obstetrics and Gynecology Department of University Emergency Hospital Bucharest. We studied the incidence, prevalence and distributions of some of the most frequent thrombosis-associated genetic mutations: factor V Leiden, factor V H1299R, prothrombin gene, C677T and A1298C mutations which determine methylenetetrahydrofolate reductase deficiency (MTHFR), factor XII, PAI-1, G4600A and C4678G mutations of endothelial protein C receptor. **Results:** In accordance with the data so far, the prevalence of factor V Leiden G1691A mutation was 10,54% (n=48), all as heterozygous GA state. For the homozygous state, we encountered a single case (0,21%), but having the H1299R AG mutation. We found a higher prevalence for the prothrombin G20210A gene mutation compared to the one reported so far, of 4,39% (n=20). The association of FV Leiden with other thrombophilic factors was reported in 40 cases (10,54%). We encountered 6 cases (1,31%) of compound heterozygosity for the factor V and prothrombin mutations, representing a highly thrombogenic state. Also, the reported cases for MTHFR C677T were similar with the literature, regarding the prevalence – 56,7% (n=258), representing patients at low risk for thrombosis. We also report 88 cases (19,3%) of homozygous state for MTHFR C677T and 84 cases (18,4%) with double heterozygous, MTHFR C677T and A1298c which increases the risk of hyper-homo-cysteinemia, as well as homozygosity for the 4G/4G mutation in type 1 PAI – 13 cases (2,85%). **Conclusion:** Tests for thrombophilia should be carried out in women with personal pathological and/or obstetrical history, planning for a pregnancy, in order to establish an adequate prophylaxis method. Knowing the thrombophilic state of a patient is essential in order to decrease maternal and fetal morbidity and mortality.

P034

MANAGEMENT PRACTICE PATTERN FOR PRETERM LABOR IN INDIA – A MULTI-CENTRIC STUDY

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Problem statement: Given the enormity of burden posed by preterm labor (PTL) on Indian society, a closer scrutiny of the current clinical management practices of PTL is not bereft of scientific merit. As clinical diagnosis remains the mainstay in the management of PTL, an attempt was done in this study to understand the clinical and obstetrics characteristics of PTL patients with respect to cervical dilatation. **Methods:** Case records of patients with spontaneous preterm labor (24-37 weeks of gestation), as diagnosed by the physician, were included for evaluation in this retrospective study. Data pertaining to obstetric history profile, clinical and obstetrics characteristics of PTL patients with respect to cervical dilatation (2cm), latency period with various

tocolytics (pharmacological) and the comparative characteristics of patients who were on non-pharmacological management (non tocolytic therapy) were assessed. **Results:** Data from 285 patients (mean age: 26.28±4.62 years) were included in this analyses. Mean (±SD) gestational age at time of onset of PTL in isoxsuprine and nifedipine group was 31.90 (±3.39) and 33.29 (±2.37) weeks in patients with 2 cm cervical dilatation. Average latency period in isoxsuprine and nifedipine group was 25.09 (±26.02) and 4.90 (±8.86) days in patients with cervical dilatation of 2cm; whereas it was 8.11 (±18.39) and 1.15 (±1.28) days in patients with 2cm cervical dilatation, respectively. Mean (±SD) latency period for the non-pharmacological group was 1.52±6.56 days. Significant difference was noted between pharmacological (tocolytic group) and non-pharmacological group (non-tocolytic) (p0.05; chi square test). **Conclusions:** Pharmacological treatment was preferred for the management of PTL in India. Significant difference in terms of latency period was evident for pharmacological over non-pharmacological group. In cervical dilatation (2 cm) latency period was better in isoxsuprine compared to nifedipine group. **Disclosure:** This study was funded by Abbott India Ltd. Dr Jaju, Dr Sood, Dr Chavan and Dr Devgarha received research funding from Abbott India Ltd.

P035

EFFECT OF LYCOPENE ON LEVEL OF PLACENTAL GROWTH FACTOR (PIGF) IN PREECLAMPSIA-INDUCED PLACENTAL TROPHOBLAST CELLS

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Preeclampsia is a major cause in both maternal and perinatal mortality and morbidity. Underlying mechanism of preeclampsia remains unclear. It is assumed that preeclampsia is caused by imbalance in angiogenesis and antioxidant in blood and placenta. Lycopene, known to possess antioxidant properties and to maintain body stability in spite of changes, is therefore a promising agent to decrease preeclampsia risk. This study aimed to observe lycopene on PIGF level in placental trophoblast which is induced by preeclampsia *in vitro*. Level of PIGF was measured with ELISA method. In preeclampsia-induced trophoblast, PIGF level significantly increased (p0,001) after treated with lycopene of 15.625 µg/ml incubated for 24 hours. Lycopene possess high antioxidant and balance in angiogenesis factor that plays role as precursor in scavenging reactive oxygen and reduce free radicals that recover trophoblast cells induced by preeclampsia as indicated by increase in PIGF level. Further studies regarding the optimal concentration of lycopene on embryo cell for clinical trial, are encouraged. **Keywords:** angiogenesis, lycopene, preeclampsia-induced trophoblast, PIGF

P036

GENETIC PREDISPOSITION AND MATERNAL INFECTION AS A RISK FACTORS OF SEVERE PREECLAMPSIA

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Problem statement. Preeclampsia (PE) is one of the major causes of maternal and perinatal morbidity and mortality. Previous studies of the association between PE and polymorphisms of angiotensin II receptor *AGTR1*-1166AC and endothelial nitric oxide synthase



NO3-894GC have yielded conflicting results. In recent years, a growing body of literatures suggests that maternal infections play an important role in the pathogenesis of PE. The aim of the present study was to assess the association between AGTR1-1166AC and NO3-894GC gene polymorphisms, and maternal infection and risk of severe preeclampsia (SPE). **Methods.** This study included two groups of primiparous women aged 20-35 years with spontaneous singleton pregnancy: 100 patients with SPE and 100 women without PE. All women had not a history of hypertension, autoimmune, metabolic, renal, or cardiac diseases, and preeclampsia before this pregnancy. We have analyzed χ^2 , odds ratio (OR) and its 95% confidence intervals (95%CI). **Results.** We did not observe increased risk of SPE in mutant homozygotes with NO3-894CC genotype (OR=1.5, 95%CI 0.42-5.6; p=0.517). Mutant genotype AGTR1-1166CC was detected only in patients with PE (5% vs 0%, p=0.024). We found significant association between maternal systemic infectious and SPE (OR=49.6; 95%CI 13.05-188.64). The risk of SPE were significantly lower in patients with local infections of the lower genital tract (OR=4.5; 95%CI 1.49-6.71). Asymptomatic bacteriuria is associated with the highest risk of SPE (OR=17.0; 95%CI 4.66-61.81). Acute gravidarum pyelonephritis showed lower association with SPE (OR=5.4; 95%CI 1.69-10.54). We did not observe increased risk of SPE with acute respiratory infections (OR=2.0; 95%CI 0.71-4.69). Acute non-specific bacterial vaginitis was found to be risk factor of SPE (OR=6.7; 95%CI 1.90-11.02). Cytomegalovirus infection (2%), toxoplasmosis (2%), Chlamydia trachomatis cervicitis (4%), acute Trichomonas colpitis (2%) and bacterial vaginosis (4%) were found only in patients with SPE. **Conclusion.** A clear association between genetic predisposition and preeclampsia has not been established. Our data support that acute maternal infection is associated with an increased risk of severe preeclampsia. Systemic inflammatory response might be the main potential mechanisms related to infections and enhanced development of severe preeclampsia. Prompt treatment or prophylaxis against infection might reduce the risk of preeclampsia.

P037

DEVELOPING A LOW COST, MASS MARKET, NON-INVASIVE, PRENATAL DIAGNOSTIC SCREENING TEST FOR DOWNS SYNDROME USING MALDI TOF MASS SPECTROMETRY IN CHINA

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Problem Statement: Recent advances in prenatal testing are rapidly changing the way in which early pregnancies are being managed. However, aside from traditional marker assays and confirmatory amniocentesis, new tests are still the preserve of the privileged, or those who live in developed countries. Thus, despite the rapid growth of NIPT, the high cost associated with blood based DNA testing has meant that pregnancies in low/middle income countries, including China, are only tested for using invasive methods, late (sometimes in the 3rd trimester), or not at all. This is putting patients at risk, resulting in cultural stigma and leading to uninformed, underprepared healthcare decisions and provision for pregnant women. **Methods:** A simple, non-invasive, test to analyse urine using mass spectrometry has been developed in the UK and in this study the novel approach was applied to the urine collected from pregnant women in China to determine the potential sensitivity and specificity of detecting Downs syndrome in this population. Using a data set from 789 representative samples, we have

developed algorithms based on spectral regions, which contain characteristic peaks with a high discriminatory power. We validated the algorithms using an independent data set containing an additional 2095 samples from the same cohort (total cohort n=2884). **Results:** Three T21 and two T18 pregnancies were clearly identified in the cohort using spectral differences specific to each aneuploidy. The algorithms used successfully detected trisomy 21 samples with a sensitivity of 100% and with a false positive rate lower than 10%. Strikingly, when the algorithm was built to account for gestational age variation false positive rate dropped to 0%. Similar results were seen for T18. **Conclusion:** Earlier, cheaper, urine-based testing will increase the ease and availability of prenatal testing in low/medium income countries like China, enabling better informed healthcare decisions earlier in a pregnancy without having to rely solely on NIPT or traditional biomarker screening tests which require advanced and expensive infrastructure.

P038

EARLY ADMINISTRATION OF PROGESTERONE TO PREGNANT WOMAN WITH PCOS COULD BE AN IMPORTANT THERAPEUTIC ALTERNATIVE

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Introduction: It was seen that pregnant women with polycystic ovarian syndrome (PCOS) have an increased rate of early abortion. The authors of the study investigated the activity of the luteal body and the inherent therapeutic possibilities. **Materials and methods:** The research included 182 pregnant women with single pregnancy and it lasted for 4 years. The levels of progesterone (P) and estradiol (E) were detected 6-7 days after ovulation. Then, P was determined at gestational age of 5 weeks when the ultrasound diagnosis was confirmed. **Results:** Of the 182 pregnant women, 72 had PCOS and 106 didn't have PCOS. Of both lots, there were identified 24 cases of early episodes of abortion, although thrombophilia tests were normal. The P and E levels at 6-7 days after ovulation were similar. However, P values at 5 weeks of gestation showed significant differences of 33.2 ng / ml in the control group versus 26.9 ng / ml in the PCOS group (P 0,05). All pregnant women who had low P values at 5 weeks of gestation received progesterone treatment. **Conclusions:** Pregnant women with PCOS have a low P production in their first weeks of gestation. This could be correlated with a higher rate of early pregnancy loss. In conclusion, for pregnant women with PCOS, progesterone therapy can reduce the number of early abortions.

P039

THE RELATIONSHIP BETWEEN PERIODONTAL DISEASE AND DELIVERY PROCESS; A CASE-CONTROL STUDY

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Objective: Preterm birth is defined as any delivery that occurs after 23 gestational weeks and less than 37 weeks. There is convincing evidence that infections in pregnant women may result in preterm labor. The aim of this study is to assess the relationship between

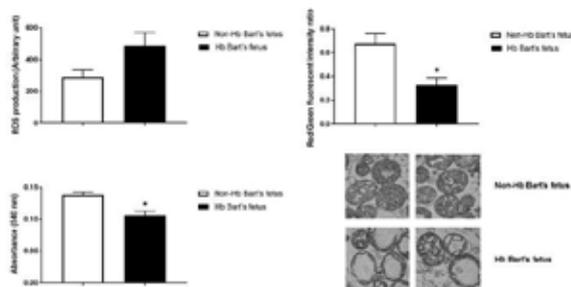
preterm birth and periodontal disease in pregnant women in Jahrom city, Iran. **Methods:** in case-control study on 120 pregnant women was performed as a random sampling. According to gestational age, participants were divided into case and control groups. Case group includes parturient women with preterm birth and control group were those with term delivery. All pregnant women were under dental examinations, then their periodontal disorders was calculated and scaled. The data analyzed by SPSS 21 and Chi-square software. **Results:** The average age of pregnant women is 28 years. The mean head circumference of the neonates is 34 cm, height 48.6 cm, and weight 3133 g. 4.1% of women with periodontal disease had preterm delivery. Most of them had normal vaginal delivery. **Conclusions:** In contrast to other studies, most people with periodontal disease had normal vaginal delivery. In this study, We find out that cultural and economic status of the community play an important role in the prevention of dental diseases, however, there was no relationship between periodontal disease and preterm labor. As its shown in our results, Factors affecting early delivery are still unknown and more study should be done for better conclusion. **Keywords:** Periodontal disease, Pregnant women, Preterm delivery.

P040
MITOCHONDRIAL FUNCTION IN CARDIAC TISSUE OF THE FETUSES AFFECTED BY HEMOGLOBIN BART'S DISEASE

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Figure 1: Mitochondrial function and Cardiac mitochondrial morphology by transmission electron microscopy (EM)



Problem statement: Hemoglobin (Hb) Bart's disease is the most severe spectrum of thalassemia disease. The fetuses affected by Hb Bart's disease develop hydrops in utero. The cause of fetal cardiac failure is most likely one of the following: volume overload status, cardiac tissue hypoxia or iron accumulation. The theory of cardiac failure in fetal Hb Bart's disease is not yet established.

Objective: To compare mitochondrial function, levels of iron accumulation, inflammatory markers and apoptosis markers in the fetal cardiac tissue between Hemoglobin Bart's fetuses and non-hemoglobin Bart's fetuses. **Methods:** A cross-sectional analytic study was conducted on two groups of fetuses including fetuses affected by hemoglobin Bart's disease (Study group) and those of non-hemoglobin Bart's diseases (Control group). In all fetuses were performed cardiac function ultrasound and then cardiac tissue from the left ventricle were collected after termination of pregnancy for measurements of iron accumulation levels, mitochondrial function (mitochondrial swelling, reactive oxygen species (ROS) production levels, and JC-1), inflammatory process markers such as TNF- α (inflammatory marker) and apoptosis process markers (Bcl-2 and active caspase-3). **Result:** A total of 28 fetuses meeting the inclusion criteria consisted of 18 fetuses affected by hemoglobin Bart's disease and 10 non-affected fetuses. At 18-22

weeks of gestation, the iron accumulation level in cardiac tissue was not significantly different ($P=0.662$). Mitochondrial function in fetal cardiac tissue swelling and JC-1 were significantly higher in the study group ($P=0.008$ and $P=0.012$). In the Hb Bart's fetuses, the inflammatory marker (TNF- α) was significantly higher ($P=0.045$). Additionally, apoptotic marker (active caspase-3) and anti-apoptotic marker (Bcl-2) were also increased significantly ($P=0.001$ and $p=0.035$). **Conclusion:** The mitochondrial function was significantly decreased in fetuses with hemoglobin Bart's disease, even in the early second trimester. However, an iron accumulation in cardiac tissue was not different in both groups. The findings suggest that myocardial cell damage in fetuses with hemoglobin Bart's disease may be primarily caused by anemic hypoxia rather than iron overload. **Conflict of interest:** The author declares that there is no conflict of interest. **Keyword:** Mitochondrial function, Hemoglobin Bart's fetus, Cardiac tissue

P041
OVARIAN VEIN THROMBOSIS- A RARE CAUSE OF ABDOMINAL PAIN IN POSTPARTUM WOMEN

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Problem Statement: Ovarian vein thrombosis (OVT) is a rare but potentially serious postpartum complication that may mimic a surgical abdomen. It is an uncommon finding occurring in 0.05% to 0.18% of pregnancies. In this report, we present the case of a 22-year-old primigravid patient who developed OVT after an emergency caesarean section. **Methods:** TK had an uncomplicated caesarean section after a failed instrumental delivery and was discharged home 48 hours later. She however presented 12 days postpartum complaining of severe abdominal pain and fever. The differential diagnosis included a surgical abdomen, pyelonephritis and pelvic collection. TK had a full septic screening and was commenced on intravenous antibiotics and a computerised tomography (CT) scan was requested. **Results:** TK's white cell count was $14.7 \times 10^9/L$ and C-reactive protein 315 g/L. On examination she was noted to have fullness around pelvis, peritonism in lower abdomen and bilateral flank tenderness. CT showed bilateral ovarian vein thrombosis and possible endometritis. TK was commenced on treatment dose of LMWH as per the advice of the haematologist. She was referred to anticoagulation team with a follow up in their thrombosis clinic and was to continue the LMWH until her appointment. **Conclusion:** The diagnosis of OVT can be made with confidence using radiological imaging. Management is necessary to avoid the morbidity and mortality associated such as pulmonary embolism, sepsis, and even death. Treatment is particularly important in the post-partum patients, with anticoagulation therapy being the current recommendation.

P042
ASSOCIATION OF CEREBROPLACENTAL RATIO AND PLACENTAL VASCULAR MALPERFUSION IN NORMALLY GROWN FETUSES

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Problem statement: To investigate the use of fetal cerebroplacental ratio (CPR) to identify placental vascular malperfusion. **Methods:** Sixty-five full-term pregnant women were studied prospectively in the third trimester of pregnancy. Doppler ultrasound examination of umbilical artery (UA), middle cerebral artery (MCA), and uterine artery (UtA) was performed at 35-40 gestational weeks. The pulsatility index (PI) was calculated. The CPR was calculated as the ratio between the MCS PI and the UA



PI. All Doppler indices were converted into multiples of median (MoM), correcting for gestational age using reference ranges. CPR 0.6765 MoM was regarded as abnormal value. All Doppler indices were converted into multiples of median (MoM), correcting for gestational age using reference ranges. Histological characteristics of placentas were classified as normal, histological chorioamnionitis, and vascular underperfusion. **Results:** The CPR values of fetuses were not significantly associated with abnormal pathologic findings. Fetuses with an abnormal CPR value were significantly more likely to have an adverse composite perinatal outcome and higher rates of cesarean delivery. Cord gas analysis was not associated with low CPR value. **Conclusion:** A low CPR was associated with increased rates of adverse composite perinatal outcome, but not associated with abnormal pathologic findings.

P043

COMPARISON BETWEEN HYSTERECTOMY AND NON-HYSTERECTOMY AFTER UTERINE ARTERY EMBOLIZATION COMPLICATED INFARCTION

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Problem statement: Uterine embolization is a less invasive vascular radiologic technique for postpartum bleeding control, but rarely, it can cause uterine infarction. To manage infection from necrotic tissues, there are several methods including antibiotics therapy, curettage, and hysterectomy. Physicians should consider whether the assessment and management for uterine infarction is good. **Methods:** In our hospital, we report two cases of postpartum hemorrhage which was treated by uterine artery embolization but uterine infarction was complicated. One patient spared the uterus but the other patient had hysterectomy. **Results:** Both patients were first managed with broad spectrum intravenous antibiotics and after one month, one patient had open hysterectomy. After surgery she was discharged without complications. Other patient used more antibiotics and intermittently admitted, debriment and vaginal dressing were done. She quit antibiotics 2 months later and no more vaginal discharge was present. **Conclusion:** Uterine infarction after embolization is usually diagnosed after 3-4 weeks, and patients were presented with fever, leukorhrea or abdominal pain. Uterine necrosis worsens patient's physiological psychological quality of life and needs additional procedure. When hysterectomy is done, antibiotics use afterward is no longer than 2 days but without hysterectomy, patients need various antibiotics use for various infection causes. Both cases couldn't secure fertility because of the endometrium had complete necrotic change but the patient who didn't have hysterectomy was also satisfied with conservative management because she didn't want no more surgical procedure. The important factor in managing this rare complication is accurate assessment about patient's symptoms and fast decision in addition to relationship and communication between obstetrician and patients.

P044

THE SIGNIFICANCE OF GESTATION CORRECTED HYPERURICEMIA AS PREDICTORS OF THE RECURRENCE OF PREECLAMPSIA ON SUBSEQUENT PREGNANCY

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Problem statement: Hyperuricemia has been described commonly in preeclamptic pregnancies, often preceding the diagnosis of preeclampsia and historically was used as a diagnostic marker of preeclampsia. The aim of this study was to determine the usefulness of gestation corrected hyperuricemia to

predict the recurrence of preeclampsia on subsequent pregnancy. **Methods:** The retrospective study of 64 women who had previous preeclampsia and checked serum uric acid was analyzed. Gestation corrected hyperuricemia (GCH) was defined as being one standard deviation above the gestation-specific mean. And we used uric acid z-scores ([serum uric acid value - gestation specific mean] / standard deviation of the population) to account for gestation-specific alterations in uric acid and tested this as a continuous variable. The relationship between GCH and recurrence of preeclampsia on subsequent pregnancy was analyzed. Obstetric outcomes were reviewed according to absence or presence of GCH. **P Results:** Of 64 women, seventeen had the development of recurrent preeclampsia (26.6%). The absence or presence of GCH was not associated with the recurrence of preeclampsia on subsequent pregnancy ($p=0.267$). And gestation-specific uric acid z-score as a continuous variable did not show any association with the prediction of preeclampsia on subsequent pregnancy ($p=0.427$). GCH was associated with the small for gestational age ($p=0.010$). **Conclusion:** GCH does not predict the recurrence of preeclampsia on subsequent pregnancy.

P045

THROMBIN STIMULATES EXPRESSION AND SECRETION OF MONOCYTE CHEMOTACTIC PROTEIN-1 (MCP1) AND INHIBITS ANGIOGENESIS IN EXTRAVILLOUS TROPHOBLAST

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Problem statement: Inadequate placentation causes recurring miscarriage and pregnancy loss. **Methods:** Cell Culture, Tube formation assay, ELISA, MCP-1 silencing, RNA isolation, and real-time PCR. **Results:** We report that Thrombin exclusively regulates secretion of MCP-1 in HTR-8/SVneo trophoblast cells. Interestingly, we found that Thrombin regulates MCP-1 protein secretion in 6 hours and gene expression within 12 hours of treatment. Moreover, MCP-1 secretion was controlled by Rac-1 and Rho/Rho kinase in 12 hours. Further, the ability of tube formation of HTR-8/SVneo cells is regulated by Thrombin via MCP-1 dependent manner. **Conclusion:** In summary, the data reported here provide evidence that Thrombin might apparently have a negative impact on the ability of Endovascular Trophoblast to generate the capillary system which seems to be regulated by MCP-1. **Keyword:** MCP-1, Thrombin, HTR-8/SVneo trophoblast cells. **Disclosure of Interest:** The authors declare that they have no disclosure of interest.

P046

EVALUATION AND ANALYSIS OF ACCURACY OF PRENATAL DIAGNOSIS IN CONGENITAL DISEASES BY IMAGING EXAMINATION

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Problem statement: The aim was to assess the correlation between fetal ultrasound (US) diagnosis of congenital diseases and identification of patients needing urgent postnatal therapy. We examined the accuracy of prenatal ultrasound diagnosis at an urban referral center. **Methods:** A prospective study on 335 fetuses in singleton pregnancies found 12 fetuses with congenital diseases and a control group of 323 fetuses with a normal ultrasound examination. All fetuses underwent a detailed ultrasound scan and a full biometric evaluation. **Results:** The mean

maternal age, obstetrical history, mode of conception or fetal gender didn't differ between the groups. The ultrasound pathological aspects were:- isolated borderline ventriculomegaly – 1 case, related to other larger fetal biometric measurements and does not mean a pathological condition. - nuchal translucency (NT) above 3.5 mm when the crown-rump length measures between 45 and 84 mm – 2 cases. The prognosis was poor because the association with karyotype abnormalities. - perimembranous (pVSD) and muscular (mVSD) ventricular septal defects– 2 cases. Fetus with isolated pVSD presented more pronounced right ventricular dominance as compared to mVSD, with no differences in biventricular function at third trimester echocardiography.- unilateral intracardiac foci in the left ventricle – 6 cases, commonly seen inside heart chambers during routine fetal heart scanning, the left ventricle being the most frequent location. They represented a normal variant of papillary muscle development, without congenital heart defects. - abnormal karyotype – XO – Turner syndrome – 1 case, affected the phenotype of the fetus but it may not reliably predict the clinical presentation. **Conclusion:** Future studies are warranted to confirm these findings for better understanding of pathophysiological mechanisms underlying prenatal diagnosis in congenital diseases by imaging examination.

P047

A LOCAL RISK SCORE MODEL FOR VENOUS THROMBOEMBOLISM PROPHYLAXIS FOR CAESAREAN SECTION IN CHINESE WOMEN AND COMPARISON WITH INTERNATIONAL GUIDELINES

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Problem statement: Recommendations for venous thromboembolism (VTE) prophylaxis from authoritative guidelines for women undergoing caesarean delivery differed significantly and may not be applicable to Chinese populations. We aim to formulate a local risk model for VTE prophylaxis for caesarean section women. **Methods:** A local risk score model based on demographic, obstetric and medical parameters was used to assess the risk of VTE in women undergoing caesarean delivery from May 2017 to April 2018 in a regional obstetric unit. Women with increased risk (VTE Score =2) are given mechanical prophylaxis with pneumatic cuff and those with high risk (VTE Score =3) are additionally prescribed low molecular weight heparin (LMWH) as pharmacological prophylaxis in the early postpartum period. The risk scores obtained by applying other major guidelines were then compared. **Results:** Of 859 patients were included for analysis, overweight (15.3%), advanced maternal age (9.7%), multiple pregnancy (5.1%), obesity (4.7%), and primary postpartum haemorrhage (4.1%) were the most common risk factors. Overall, 109 (12.7%) patients required mechanical prophylaxis and 28 (3.3%) patients required additional pharmacological prophylaxis. No patient had postpartum VTE events nor serious haemorrhage after receiving LMWH prophylaxis. In contrast, applying the Royal College of Obstetricians and Gynaecologists guidelines to our cohort, 649 (75.6%) patients would receive LMWH after caesarean section, compared with no patients under the American College of Obstetrics and Gynaecology guidelines. **Conclusion:** Our local risk score model avoided the need for large proportions of women to be subjected to pharmacological prophylaxis and appeared safe and practical.

P048

A COMPLEX MALFORMATIVE SYNDROME – AN EVEN MORE COMPLEX JARCHO-LEVIN SYNDROME?

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Problem statement: Jarcho-Levin syndrome (spondylocostal dysplasia) is a rare condition, with a prevalence of 1/200.000 births, characterized by vertebral and rib segmentation defects and associated with a high mortality rate in the first few months of life due to respiratory failure. Other internal abnormalities have been associated to the syndrome, including neural tube defects, genitourinary abnormalities and diaphragmatic hernias. **Methods:** Description of a clinical case. **Results:** A 31-year-old woman, multiparous, apparently healthy (except for positivity for Hepatitis B antigen) presented at the hospital at 16 weeks of gestation for prenatal diagnosis after being detected a fetal nuchal translucency of 3.1mm (above the 95th percentile) in the first trimester ultrasound. Combined first-trimester screening (maternal age, ultrasound and biochemistry – PAPP-A and free β -hCG) was negative. An amniocentesis was performed with a normal karyotype result (46,XY). Fetal echocardiography at 22 weeks suggested a subaortic intraventricular communication. Obstetric ultrasound at 23 weeks revealed a neural tube defect with cyphoscoliosis, associated with left diaphragmatic hernia, non-visible bladder, ambiguous genitals and polyhydramnios. The patient opted for pregnancy termination. Anatomic pathology fetal exam revealed a complex polymalformative syndrome, involving hypoplasia and asymmetry of the trunk (Sprengel deformity), multiple anomalies of thoracic vertebrae with medullary lesion, Arnold-Chiari malformation, bilateral pulmonary hypoplasia, as well as left diaphragmatic hernia, polysplenia, severe genitourinary anomalies with bladder extrophy and absence of external sexual organs. **Conclusions:** The clinical case presented could correspond to Jarcho-Levin syndrome with a wide range of associated complex internal abnormalities (besides skeletal abnormalities). This case reveals a scenario in which prenatal diagnosis was fulcral for the early detection of severe fetal malformations, preventing severe neonatal outcomes. Furthermore, it elucidates the importance of an integrated prenatal diagnosis, despite having a normal karyotype.



P049

DANDY-WALKER COMPLEX: A CASE REPORT OF PRENATAL DIAGNOSIS OF DANDY-WALKER VARIANT

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Problem statement: The Dandy-Walker complex comprises a heterogeneous spectrum of rare congenital intracranial malformations (prevalence of 1/30.000 births). It is classically characterized by agenesis/hypoplasia of the cerebellar vermis, dilation of the fourth ventricle and enlargement of the posterior fossa (Dandy-Walker malformation). Other diseases included in the spectrum are Dandy-Walker variant (hypoplasia of the cerebellar vermis and absence of enlargement of the posterior fossa) and Megacisterna magna (enlarged cisterna magna with normal cerebellar vermis and fourth ventricle). Complications are related to hydrocephaly and neurodevelopmental disorders. Prenatal diagnosis of this condition may be possible through obstetric ultrasound or fetal brain imaging. **Methods:** Description of a clinical case. **Results:** A 35-year-old pregnant woman, previously healthy, multiparous with a previous caesarean delivery, presented at our hospital at the 33rd week of gestation following the detection of abnormalities in the ultrasound of the third trimester, including fetal growth restriction and enlargement of the cisterna magna. Previous exams during pregnancy were unremarkable. She was admitted for investigation and surveillance of maternal and fetal well-being. Ultrasound performed at the 34th week revealed a fetal growth restriction (5th fetal growth percentile, with normal Doppler evaluation). Furthermore, it revealed agenesis/hypoplasia of the cerebellar vermis and enlargement of the cisterna magna. Dandy-Walker complex was considered. No abnormalities were found in the fetal echocardiogram. Induction of pulmonary maturation was performed. Fetal magnetic resonance imaging at 34 weeks described a retrocerebellar cyst communicating with the fourth ventricle and a cerebellar vermis with biometry inferior to the 10th percentile, without reference to posterior fossa enlargement, favoring the diagnosis of Dandy-Walker variant, however differential diagnosis with Blakes's pouch cyst is imposed. Close maternal and fetal surveillance was performed and an elective caesarean delivery at 37 weeks was planned, due to the fetal growth restriction and previous caesarean delivery. **Conclusions:** This case illustrates the possibility of prenatal diagnosis of a rare intracerebral malformation. Due to the variability of its phenotype, both intracranial and extracranial anomalies should be excluded. Additional post-natal investigation, including brain imaging, is recommended to confirm the diagnosis and assess for complications. A multidisciplinary approach is required for follow-up and treatment.

P050

COMPLICATIONS OF ENDOMETRIOSIS DURING PREGNANCY CASE REPORTS OF LIFE-THREATENING EVENTS, LITERATURE ANNO 2018 AND THE LACK OF WELL DESIGNED TRIALS.

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Problem Statement:

- Risks of complications associated with endometriosis during the pregnancy is clearly underestimated by most of the clinicians.
- Complete lack of large epidemiological studies quantifying the incidence of complications in the population of pregnant women with endometriosis.
- These complications are rare but represent life-threatening conditions, for both the mother and the fetus, that mostly require surgical intervention (hemoperitoneum, bowel perforation, uterine rupture, placenta previa, perinatal deaths). Incidences remain clearly underestimated with maximum values during second/third trimester but have been occasionally reported after birth.

Methods:

- Retrospective review of 2 cases, in a period of 16 months, with strong similarities. Medical record findings were summarized and compared.
- Published literature was reviewed using Pubmed, Cochrane Library and Up-to-date looking for the words endometriosis, pregnancy, complications, life-threatening.

Results (case reports):

Reference	Year	Study type	Abstracts	Study Design	Conception	Pregnancy course	Symptoms	Intervention	Outcome	Results
1	2018	Case report	• 33 rd week of gestation • 35 th week of gestation • 37 th week of gestation • 39 th week of gestation	Case	Spontaneous	• Unremarkable until 33 rd week • Adhesions for previous caesarean • No placental abnormalities	• Heavy abdominal pain • Hemoperitoneum • Bowel perforation • Uterine rupture	• Median laparotomy • Hemoperitoneum • Bowel resection • Uterine preservation	• Perinatal fetal death • Maternal survival	• Normal placental and fetal anatomy/pathological results • Pathological identification of endometriosis nodules
2	2017	Case report	• 33 rd week of gestation • 35 th week of gestation • 37 th week of gestation • 39 th week of gestation	Case	Spontaneous	• Unremarkable until 33 rd week • Adhesions for previous caesarean • No placental abnormalities	• Heavy abdominal pain • Hemoperitoneum • Bowel perforation • Uterine rupture	• Median laparotomy • Hemoperitoneum • Bowel resection • Uterine preservation	• Perinatal fetal death • Maternal survival	• Normal placental and fetal anatomy/pathological results • Pathological identification of endometriosis nodules

Results (literature):

Number of publications: 142

Reported complications:

- 39 hemoperitoneum (as consequence of vascular rupture or abnormal angiogenesis)
- 17 intestinal perforations (after endometriosis tissue invasion)
- 14 ruptures of endometriomas
- 10 acute appendicitis connected to appendiceal endometriosis
- 2 uroperitoneum
- 2 distortions of renal system anatomy
- 63 uterine ruptures (all of the reported cases underwent pelvic surgery)

Conclusion:

- Complications of endometriosis during pregnancy are rare but life-threatening conditions
- Pathophysiological explanation remains hypothetical:
- endometriosis-related chronic inflammation: makes tissues and vessels more friable
- adhesions: increasing traction on surrounding structures when uterus is enlarging
- Invasion of healthy structures by decidualized endometriotic tissue with subsequent risks of tissue rupture or haemorrhage.
- Strongest evidence: association between endometriosis and higher rates of placenta previa.



- Controversial: association with increased risk of miscarriage, intrauterine growth restriction, preterm birth and hypertensive disorders.
- No clear evidence for benefits of prophylactic surgery on maternal and fetal outcome.
- Need to correlate occurrence of obstetric complications with the stage of the disease in order to identify patients with increased risks of severe complications.

P051

USE OF ATOSIBAN: SAFETY EVALUATION STUDY RELATED TO TOTAL DOSE ADMINISTERED IN THREATENED PRETERM LABOR

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Problem statement: The prevention of preterm delivery is one of the primary goals of obstetricians and safety of tocolytic agents is an enduring matter of concern of them. Atosiban is a competitive vasopressin/oxytocin receptor antagonist and atosiban functions as a mixed vasopressin (V1a) and oxytocin receptor antagonist. In South Korea, use of atosiban has become increased for last 12 years. Its favorable acceptance may be due to its placebo level side effects and maintenance therapy with atosiban has often been used to prolong uterine quiescence these days. However, inhibitory effect on vasopressin receptor have never been satisfactorily resolved and no clinical studies have clearly demonstrated the side effects of multiple-cycle treatment, especially more than 3 cycles. The objective of this study is to evaluate the effect of multiple cycle atosiban therapy on mother and fetus. **Methods:** We retrospectively sampled data on 671 women hospitalized for preterm labor (24-35 weeks' gestation) in our centers between 2012 and 2017. All patients were subjected to tocolysis with atosiban. Of the 671 cases, patients who received combination therapy with ritodrine were excluded from the analysis. Remaining 369 patients were divided into 2 groups on the basis of whether or not ≥ 4 cycles of atosiban were administered. Possible maternal adverse events and neonatal morbidity were assessed. **Results:** We had 369 women received treatment with atosiban as a single tocolytic agent during hospitalization. Perinatal outcome data were available for 309 babies. 294 patients underwent 1 to 3 cycles (group A). The majority of women received single cycle treatment ($n=128, 34.7\%$). 75 patients underwent 4 to 6 cycles (group B). There was no report of serious maternal adverse events such as cardiopulmonary event. No statistical difference in neonatal outcomes were observed in either group. all cases admitted to the neonatal intensive care unit were deemed unlikely to be related to multiple atosiban treatment. **Conclusions:** We believe that the result of this study could provide more evidence on the safety of using multi-atosiban tocolytic therapy in pregnancy with preterm labor.

P052

A LARGE NEONATAL SACROCOCCYGEAL TERATOMA
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Problem Statement: Sacrococcygeal teratoma (SCT) is the most common congenital tumour in the neonate. They are composed of cells, which arise from all three germinal layers, with an incidence of 1-2 per 27,000 deliveries. They are more common in females than in males (3 to 4: 1) but are often malignant in boys. Prenatal diagnosis typically occurs in the second trimester, and Altman type I or II are the most obvious on in utero ultrasound. **Methods:** A case report of a neonate is presented with a review of the literature on prenatal diagnosis and management. **Results:** A five -day old female baby was born by normal vaginal delivery with a 10 x 10cm large sacrococcygeal lump. The tumour consisted of solid and

cystic components. She underwent a complete surgical resection of the teratoma with an uneventful postoperative period. Two- year follow-up with serum alpha-fetoprotein and surveillance imaging showed no evidence of tumour recurrence. **Conclusion:** SCTs are seen as a mass near the distal spine on prenatal sonography and can be associated with other structural abnormalities. The most important differential diagnosis is a distant neural tube defect. The main goal of serial ultrasounds is to identify hydrops fetalis, which can result in intrauterine fetal death. Rapidly enlarging tumours, tumours with predominantly solid components and large vascular lesions increase perinatal mortality. In utero interventions are temporary measures to decrease the impact of the teratoma on the fetus. Complete surgical resection is the cornerstone for definitive management of benign SCTs.



P053

CERVICAL ECTOPIC PREGNANCY: A CASE REPORT

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Ectopic cervical pregnancy is an extremely rare phenomenon caused by implantation of zygotes in the endocervical mucosa and the development of pregnancy in that unfavorable place. Early diagnosis and nonsurgical management are required in order to preserve fertility and help in decreasing maternal mortality and morbidity. We report two cases of CEP and the challenges in the diagnosis and management are discussed. A 30-year-old primigravida referred as a case of missed abortion with mild vaginal bleeding of 7 days duration following 9 weeks amenorrhea. Clinical examination revealed ballooning of cervix with partially open external os. Serum β hCG level- 3992 mIU/ml . TV ultrasound scan revealed empty uterine cavity, closed internal os and a heterogeneous space occupying lesion, enlarged and spongy cervix filled with coagulum and mass indicating an ovular tissue. A 33-year-old, second gravida with previous lower segment C-section, presented with painful abdomen and vaginal bleeding following 6 weeks of amenorrhea. The case was diagnosed as CEP. On gentle per vaginam examination, there was ballooning of cervix with a patulous external os. TV scan revealed empty uterine cavity with endometrial thickness 8 mm, product of conception in the cervical canal, gestational sac containing live embryo of 6 weeks gestational age. Both the ovaries and tubes were normal and there was no free fluid in pouch of Douglas. Serum β hCG level- 15908mIU/ml. Provisional diagnosis of CEP were made in both of cases. Mifepristone tbl. in a dose of 200 mg and Misoprostol tbl.



400 mcg were given orally followed by the minimal invasive procedure- curettage in view of intractable bleeding to save the patient life. Patients were discharged and advised for weekly follow-up with β hCG. Follow-up ultrasound revealed complete resolution. Histopathology reports confirmed the diagnosis. Patients resumed their normal periods after 2 months. There is an excellent evidence of efficacy up to 63 days of gestation using the mentioned regimens of Mifepristone orally followed by Misoprostol administration in 24 to 72 h. Women then return 4 to 14 days later for a clinical evaluation to document complete abortion. Success rates for these regimens range from 95% to 98%.

P054

THE SIGNIFICANCE OF PRENATAL ULTRASONOGRAPHIC DIAGNOSIS OF A QUADRUPLE NUCHAL CORD ENTANGLEMENT AND ITS EFFECTS ON LABOUR AND NEONATAL OUTCOME IN PROLONGED PREGNANCY – A CASE REPORT

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Introduction: The importance of nuchal cord on the management of third trimester pregnancy and labor has been debated for many years. The treatise De Octimestri Partu, by Hippocrates points to the significance of a nuchal cord entanglement. This coiling was marked as „a danger of the eighth month“. Crawford concluded that the incidence of nuchal cords rises after 38 WKS gestation, possibly reflecting greater fetal activity or decreased amniotic fluid volume. Multiple nuchal cord, especially four or more loops, demands special care due to the risk of intermittent cord compression. If signs of fetal stress are accentuated, an operative delivery may be required. **Case report:** The ultrasound findings, management, and outcome in a case of a four-loop nuchal cord were presented. The patient was a 30-year-old woman, G2 P0 Ab1, at 41 WKS 3D of gestation, referred for biophysical profile, due to prolonged pregnancy, decreased fetal movement and non-reactive NST. The prenatal care and her past history other than the hypothyreosis were unremarkable. The ultrasound findings revealed there was one fetus in the uterine cavity, FHA positive. The presentation was cephalic and the placenta's location fundal. The biometrics was suitable for 41 WKS. The FW 4000 gr. Also demonstrated reduced quantity of amniotic fluid, decreased fetal movement. On color-Doppler, four loops of cord were wrapped around the neck (fig. 1).



Figure 1: Sagittal section demonstrating 4 loops of cord.

On pulse-wave Doppler, the S-D ratio was normal- 2.5. As we could assess, this was a type A looping. A C-section was performed and the prenatal diagnosis confirmed. The 4020g male baby had Apgar scores of 9/10 and did not require any special care at the nursery. The infant was discharged home in the next two days. Conclusion: We assume that in this case, the good Apgar score and outcome

are attributed to the prompt intervention on the ultrasound findings. Color Doppler is the easiest modality to count multiple loops. Ultrasonography combined with color Doppler diagnostics is the gold standard and should be the aim for future so as to provide the best perinatal management with good fetal outcome. NST nonstresstest

P055

EVALUATION OF USING PI AS A RELIABLE TOOL OF ESTIMATING DISPROPORTIONATE FETAL GROWTH

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Background: Body mass index (BMI) and neonatal ponderal index (PI) are anthropometric tools that are regularly used to estimate disproportionate growth of hypotrophic and hypertrophic newborns expressed as weight/length² ratio and weight/length³ ratio, respectively. Current data in predicting the proportionality of neonatal growth and prediction of long-term complications in newborns is insufficient. Data on PI in premature infants has shown discrepancies in regards to gestational age, and due to the high dependency to the fetal length. Therefore, BMI would represent a more reliable tool for assessing growth of premature newborns. Fetal PI has been proved to be a reliable measure in exclusion of the intrauterine growth failure. In searching for a more reliable tool used for estimating disproportionate fetal growth, regardless of their gestational age, we compared the fetal PI, neonatal PI, BMI, and birth weight values with respect to centile curves of our sample population. **Objective:** The following study analysis is aimed to examine whether fetal PI is more reliable indicator of fetal growth; comparing the anthropometric indexes of 36 hypertrophic newborns and 51 hypertrophic newborns. **Methods:** The newborn sample data has been randomly collected from the archives of the Department of Obstetrics and Gynecology of University Hospital Centre Sestre Milosrdnice in 2018. Given data of 87 newborns has been analyzed: 59% were hypertrophic newborns and 41% were hypotrophic newborns. Statistical analysis has been performed using the SPSS.V19. FGR is defined as weight below the 10th percentile for gestational age, according to WHO Data. Similarly, hypertrophic newborns are considered those above the 10th percentile for gestational age. Fetal PI was calculated by dividing the estimated fetal weight by third power of the femur length. **Results:** Chi- squared test on a sample of 36 newborns found no connection between prenatal suspicion of FGR and postnatally confirmed FGR ($\chi^2 = 1.694$; $p.05$ $\Phi = -217$). Furthermore, we found no connection between prenatal suspicion of fetal ultrasound examination and confirmed diagnosis after birth in the sample of 51 hypertrophic newborns ($\chi^2 = .023$; $p .05$, $\Phi = -.21$, $p .05$) **Conclusion:** Fetal PI should be considered once again as a predictor of postnatal outcome.

P056

IMPACT OF EXCESSIVE MATERNAL WEIGHT GAIN DURING PREGNANCY ON ACCURACY OF PREDICTING FETAL WEIGHT

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Background: The fetal ultrasound scan in third trimester of pregnancy is a valuable tool in identifying risk factors that could potentially impare labour and delivery outcome. Maternal obesity and excessive weight gain in pregnancy are common concomitant risk factors that can significantly interfere with the appropriate fetal ultrasound evaluation. The prevalence of obesity has increased

over the past decade. According to Eurostat data, obesity and weight problems affected 51.6 % of the population (age 18 and above) among EU Member States in 2014. From the last Eurostat data in 2014, European Union has 30 % of overweight and 9.9 % of obese females in reproductive age from 25 to 34 years. The same percentage was higher in females aged 35 to 44 years (EU has 38 % overweight females and 13.1 % obese females). Body mass index (BMI) is still used as an anthropometric tool in assessing pre-pregnancy weight status and identifies pregnant women prone to excessive weight gain. Current data suggests that there is a linear relationship between patients BMI and ultrasound image quality for non-pregnant patients. **Objective:** The aim of study was to quantify the relationship between excessive maternal weight gain based on the prepregnancy BMI and the accuracy of predicting the estimated fetal weight. **Methods:** The data has been randomly collected from the archives of the Department of Obstetrics and Gynecology of University Hospital Centre Sestre Milosrdnice in 2018. Data population included 100 samples. According to the ACOG Guidelines (The American College of Obstetricians and Gynecologists) on Weight Gain During Pregnancy, the subjects were divided into groups based on pre-pregnancy BMI: under 18.5, BMI 18.5–24.9, BMI, 25–29.9 and BMI 30 or more. Women with multifetal pregnancies were excluded from the study. A comparison of third trimester estimated fetal weight and calculated maternal weight gain was made on the basis of maternal pre-pregnancy BMI. **Results:** Data of maternal pre-pregnancy BMI are shown as distribution of frequencies. Percentage of excessive maternal weight gain and percentage of difference in assessing fetal weight were tested comparing means. **Conclusion:** Based on results, the statistical significance in using percentage of excessive weight gain to predict the fetal weight ($p < 0.001$) is present.

P057

SEROUS RETINAL DETACHMENT IN PRE-ECLAMPSIA: A CLINICAL CASE

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Problem Statement: Serous retinal detachment is an unusual cause of visual loss in less than 1% of pre-eclampsia (PE) cases. It tends to be unilateral, diagnosed postpartum, and more prevalent in women who are primiparous and/or undergo caesarean delivery. The condition typically resolves completely and rarely causes total visual loss in the affected women. **Methods:** A retrospective study of a clinical case of serous retinal detachment at the Hospital Divino Espírito Santo (HDES) in Ponta Delgada, Portugal. **Results:** A 37-year-old pregnant woman submitted to *in vitro* fertilization with no relevant personal medical history and no previous pregnancies. The patient was admitted at 36 weeks of pregnancy diagnosed with PE and presented with high blood pressure (150/87 mmHg). Blood analysis showed Hb 11.1 g/dL and occasional proteinuria of 300 mg/dL, LDH 355 U/L and TGO 96 U/L. It was decided that if BP was above 160/110 mmHg, Nifedipine 10 mg was administered. Despite the improvement of the woman's BP on the second day of hospitalization, there was a slight worsening of blood test results. At that time, induction of labour with misoprostol was started. Due to the non-reassuring fetal state, the patient was submitted to an emergent caesarean section (CS). A female was delivered weighing 2470 g and with an Apgar Index of 10/10. On the first postoperative day, the patient presented with blurred vision and decreased visual acuity and was observed by an ophthalmologist who diagnosed a bilateral serous retinal macular detachment. On the third postoperative day, the patient had a spontaneous recovery in her visual acuity and experienced improvements in her other clinical symptoms, as well as her physical and analytical examinations. The patient was therefore discharged from the hospital medicated with nifedipine and

enoxaparin, and referred to Ophthalmology for follow-up. **Conclusion:** Pregnancies complicated by PE are associated with a worse prognosis for mother and child, hence it is important to be aware of the many complications that may arise. Most patients with retinal detachment in pregnancy-induced hypertension have full spontaneous resolution within a few weeks without any long-term complications. Medical treatment with antihypertensive drugs and steroids may be helpful.

P058

THE DIAGNOSTIC CHALLENGE OF CESAREAN SCAR PREGNANCY – A CASE REPORT

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Problem Statement: Cesarean Scar Pregnancy (CSP) is estimated to occur in about 1 in 2000 pregnancies. This entity has increased worldwide, due to the greater number of cesarean deliveries and the development of transvaginal ultrasonography. A high index of suspicion is required since CSP is often misdiagnosed as cervical pregnancy or missed abortion. The CSP may confer a high risk of maternal morbi-mortality. **Methods:** Overview of a clinical case of CSP diagnosed in São João Hospital, Porto, and review of the literature. **Results:** A 36-year-old woman, gravida 2 para 1, with one previous cesarean section, was admitted in our emergency department with 10 weeks of amenorrhea and acute abdominal pain, without blood loss or other symptoms. Her physical examination was unremarkable and the ultrasound scan showed a missed abortion. She underwent outpatient medical evacuation with misoprostol which was unsuccessful. Vacuum aspiration was performed one week later. The procedure was complicated by moderate blood loss that was responsive to sulprostone. The patient was discharged on the same day. The histologic specimen confirmed the presence of products of conception. The patient returned to our center ten days later with increased vaginal bleeding and acute abdominal pain. The transvaginal ultrasound revealed an enlarged cesarean scar with an embedded heterogeneous mass, with 48x45x53 mm, highly vascularized on Doppler scan. Moreover, the ovaries were normal and no free fluid was seen in the pouch of Douglas. Her serum beta

human chorionic globulin (hCG) was 2374mIU/mL. Considering the suspicion of CSP in an hemodynamically stable patient, she was medically treated with a single-dose of systemic methotrexate. The patient is still under follow-up at our institution, showing a decreasing trend in hCG value, despite the maintenance of the ectopic mass. **Conclusion:** This case highlights the challenge of differential diagnosis between CSP and retained gestational tissue in cesarean scar defect. Given the rarity of CSP, there are no universally established therapeutic protocols. We should consider hemodynamic stability, hCG level, pregnancy size, gestational age and desire for future pregnancy to decide the treatment plan. Whatever it is, a close follow-up is required to ensure complete resolution of pregnancy.

P059

EXUBERANT ECTOPIC DECIDUALIZATION: A CASE REPORT

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Problem Statement: Ectopic decidual transformation (or deciduosis) is a benign transient condition of pregnancy that arises from a progesterone-induced metaplasia of subserosal stromal cells. It is commonly localised in the pelvic organs serosa while the peritoneal localisation is less frequent and usually an incidental finding during caesarean section. However, decidualized tissue can grow during pregnancy and acquire a gross appearance that might mimic more serious conditions. A biopsy is necessary for establishing the diagnosis and to exclude the presence of mesothelioma, metastatic carcinoma, or peritoneal tuberculosis. We hereby report a case of extensive ectopic decidualization of the anterior surface of the uterus, discovered incidentally during a caesarean section performed due to fetal distress. **Methods:** A retrospective study of a clinical case of extensive ectopic decidualization of the uterus serosa at the Maternidade Dr. Alfredo da Costa in Lisbon, Portugal. **Results:** A 35-year-old primiparous woman with a medical past of endometriosis and an uneventful antenatal period underwent a caesarean section at term due to fetal distress. Upon delivery, the anterior uterine serosa showed an exuberant dark-red exophytic lesion, with an irregular and highly friable surface and well-defined borders, which was biopsied. Further examination of the abdominal cavity revealed no other lesions. Mother and infant were discharged from hospital on the third postoperative day without any postpartum complications. The microscopic examination of all biopsy fragments revealed similar histomorphological aspects, consistent with the diagnosis of ectopic decidual transformation. **Conclusion:** Ectopic decidua is usually found incidentally during surgery and is most commonly described in the pelvic organs serosa. Although a benign lesion that resolves with no treatment in the postpartum period, it can demonstrate an uncommon presentation and mimic more serious conditions, like a malignant growth. A histological analysis with immunohistochemistry are necessary for the diagnosis in these cases.

P060

FIRST GENERATION FREE OF THE HIV AND AIDS IN 2030: HOW TO ACHIEVE IT IN MEXICO?

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Problem Statement. The Sustainable Development Goals (SDGs) include achieving the first HIV-free generation by the year 2030. Public policies based on the person and the exercise of their rights are required. Mexico has structural problems and social determinants that hinder this objective. There are evidences that allow us to mark a route to achieve the objective. **Methods.**

Observational, descriptive study. We evaluated for 5 years, 2013-2017, the main indicators that influence the vertical transmission of HIV. Births, screening coverage in pregnancy, incidence and prevalence of infections. We propose actions to achieve control of vertical transmission and the first HIV-free generation in the year 2030, with an intermediate measurement progress in the year 2020. **Results.** In Mexico, in the period of analysis, the average number of births per year was 2.3 million and 14 thousand fetal deaths. 63.3% annual average of HIV detection coverage. The prevalence of HIV cases in pregnancy was 0.067%. The new cases of vertical transmission have gradually decreased, from 131 in 2013 to 79 in 2017. It is estimated that in 2017, 1,500 women infected with HIV became pregnant, with the risk of transmitting the infection. 36.7% do not know their serological status during pregnancy and 77% do not have social security. With antiretroviral treatment, 82% reached an undetectable viral load before birth. In a sample of 1,261 births, systematically analyzed, the overall risk of HIV transmission was 8.1%. **Conclusions.** In Mexico, the vertical transmission of HIV in the last 5 years has been reduced by 39.6%, although not consistently. To achieve the ODS 2030 in Mexico, it is necessary to increase detection coverage by 11% per year, from 2018 to 2020 and reach the 95% recommended by the WHO. To enter treatment for all women with reactive test and reduce of 8 % to 2% transmission of perinatal cases. Keep this indicator for 2 years and ask WHO for certification as a country free of vertical transmission of HIV. It includes the control of congenital syphilis and measures the serology of 14 thousand fetal deaths per year. **Conflict of interest:** Non-Declared.

P061

VERTICAL HIV TRANSMISSION IN MEXICO 1986-2017

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Problem Statement. Perinatal transmission or vertical transmission of the Human Immunodeficiency Virus (HIV) and AIDS, is the passage of HIV from an infected pregnant woman to her child, during the period of pregnancy, labor or breastfeeding. In Mexico, cases have been recorded since 1986 and the main factor that persists in the low detection of HIV in prenatal care that delays timely management. **Methods:** Observational, descriptive study of the epidemiological evolution of cases of vertical transmission in Mexico in 33 years, 1986-2017. Evaluate the behavior and distribution of the incidence in the last year and the structural problems of the health system that the generation. It analyzes provinces where perinatal HIV cases are concentrated and the challenges framed in the SDG 2030. **Results:** In 1986, the first registry of perinatal HIV with 6 cases. There was a progressive increase, reaching a maximum of 262 cases in 2006. From there, there is a sustained decrease until reaching 2017 with 79 cases, the lowest figure. An estimated underreporting of 37%, the national average of screening coverage for HIV, is 63.3%. Mexico has 32 provinces, 11 of them account for 77% of cases. The population without social security predominates 77% and low rates of human development. Only 44% of babies are diagnosed between 0 and 24 months of age. **Conclusions:** The low detection of prenatal HIV causes them to carry the virus without knowing it. There are highly active drugs and virological control and preventive interventions, elective cesarean and avoid breastfeeding, which have proven their effectiveness. Perinatal HIV can be prevented in 98%, if the mother receives timely and correct treatment. In Mexico, structural problems and social determinants that prevent accelerating impacts persist. Challenges: unify a fragmented health system and strengthen the quality of service in 11 provinces and integrate women without social security. **Conflict of interest:** Not-declared.



P062

COULD VAGINAL PROGESTERONE BE ASSOCIATED WITH THE DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS? VAGINAL PROGESTERONE: GUILTY OR NOT GUILTY

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Problem: Progesterone administration during pregnancy might pose a risk to develop gestational diabetes mellitus (GDM). Progesterone compounds can be administered orally, intramuscularly and vaginally. Studies on the diabetogenic effect of progesterone supplementation have yielded inconclusive results. To our knowledge this is the first study to evaluate the possible diabetogenic effect of vaginal progesterone administration on the incidence of GDM. **Methods:** In this retrospective case-control study, we included 190 women with singleton pregnancies at risk for preterm birth who received vaginal natural progesterone (200mg daily between gestational weeks 16+0 and 36+0) for a minimum of 4 weeks and delivered 28 weeks. The control group consisted of 242 age- and body mass index (BMI)-matched patients without progesterone administration. Patients with pre-existing diabetes, and conception after in vitro fertilisation procedure were excluded. Data were acquired from a database containing prospectively collected information. **Results:** The incidence of GDM did not differ significantly between the progesterone-treated and the control group (14.7% vs. 16.9%, respectively; $p=0.597$). In a binary regression model, patients with higher pre-pregnancy BMI (OR 1.1; $p=0.006$), and those with a family history of diabetes had a higher risk for GDM development (OR 1.8; $p=0.040$), whereas vaginal progesterone treatment had no significant influence ($p=0.580$). **Conclusion:** The use of vaginal progesterone for the prevention of recurrent preterm delivery and in women with a short cervix does not seem to be associated with an increased risk of GDM. The authors have no conflict of interest.

P063

ASSISTED REPRODUCTION TECHNIQUES (ART) IN PREGESTATIONAL DIABETES: RESULTS FROM A SINGLE REFERENCE CENTRE.

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Introduction and aims: Women with diabetes have fewer children than those without, but there are no reports from human reproduction units. Our aim was to compare women with pregestational diabetes who required ART (D-ART) with those with a spontaneous pregnancy (D-S) and to assess the response to ART in women with diabetes (D-ART) compared to those without (N-ART). **Methods:** Women with pregestational diabetes or ART who delivered at our centre (beyond 24 weeks) between January 2011 and December 2017 were included. Only the first pregnancy in the study period was included. Comparisons were made

between D-ART (n=11) and D-S (n=409), as well as with N-ART (N=873), using Student's t and chi-squared, with a significance set at $p<0.05$. Induction of labour was more frequent in D-ART [63.6% vs 59.3% $p=0.05$], as was caesarean section (45.5% vs 36.1% $p=0.05$), neonatal weight was lower [2714g (± 1434) vs 3476g (± 792) $p=0.05$] and they tended to suffer from intrauterine growth restriction more frequently (18.2 vs 3.4% $p=0.06$). Macrosomy (18.2 vs 17.3%, $p=1$), preterm delivery (67.9 vs 54.5% $p=0.3$), arterial pHp (0.05). When compared with N-ART, D-ART received a similar dose of FSH and HMG and treatment duration [12.9 \pm 5.6 vs 10.5 \pm 4.1 days $p=0.08$], but the number of oocytes in metaphase II obtained was lower (3.6 \pm 2.1 vs 6.5 \pm 3.8 $p=0.045$). **Conclusions:** Women with D-ART more often attend preconceptional care and have better glycaemic control, but have worse outcomes than D-S. D-ART tend to require longer treatment to obtain fewer oocytes than N-ART.

P064

SEVERE BILATERAL PNEUMONIA DURING PREGNANCY REQUIRING EXTRACORPOREAL OXYGENATION: A CLINICAL REPORT

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Problem statement: Extracorporeal membrane oxygenation (ECMO) is a rare necessity during pregnancy, having been reported in case reports or small case series on a total of 45 patients. The vast majority of these cases occurred in pregnant women with severe H1N1 influenza complicated by acute respiratory distress syndrome (ARDS). **Methods:** We report a case of ECMO performed on a 24 weeks pregnant woman with acute respiratory distress syndrome (ARDS). **Results:** A 28-year-old healthy primigravida, with a cigarette smoking habit, presented at 23 weeks of gestation with dyspnoea, coughing, fever, and acrocyanosis. She was admitted to the intensive care unit (ICU) shortly after arriving with a diagnosis of severe bilateral community-acquired pneumonia, showing signs of rapid clinical deterioration. She was intubated during the first day, yet continued to have a poor gas exchange. After developing acute respiratory distress syndrome, she started veno-venous ECMO as a rescue therapy at day 4. She was given a course of empirical endovenous antibiotics (an etiologic agent was not isolated). ECMO was suspended at day 17. After that, there was further clinical deterioration. A ventilator-associated pneumonia caused by *Acinetobacter baumannii* was diagnosed, requiring treatment with colistin. She responded favourably and was extubated at day 25. She left the ICU at day 29 and was admitted initially to the intermediate care unit and afterwards to the Obstetrics ward. Some complications occurred. She had anaemia requiring red blood cell transfusion. She developed critical illness myopathy and sixth nerve palsy due to hypoperfusion lesions, with progressive recovery from both situations. A reactivation of cytomegalovirus (CMV) was detected at 29 weeks and immunoglobulin was administered for vertical transmission prophylaxis. She had a vaginal delivery after labour induction at 38 weeks due to gestational hypertension and oligoamnios. The newborn presented an Apgar score of 9 at 1' and 10 at 5', weighed 2550g and was healthy and unaffected by CMV. **Conclusion:** Even if rarely necessary, ECMO might be used during pregnancy for extracorporeal life support. In the clinical case described, the respiratory failure was corrected and the situation evolved favourably, allowing for a healthy term newborn.



P065

SPONTANEOUS HEMOPERITONEUM IN PREGNANCY: REPORT OF FOUR CASES

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Problem statement: Spontaneous hemoperitoneum in pregnancy (SHiP) is a rare but serious complication with risk of maternal and foetal mortality. Despite there being some identified or presumed risk factors (namely nulliparity, endometriosis, raise in abdominal or uterine pressure due to Valsalva or polihidramnios), in most cases no triggering factor is identified. **Methods:** We report on four cases of SHiP that occurred in our institution over a 4-year period. In all of these cases, an exploratory laparotomy was performed. **Results:** Case 1: A 24 week primigravida (after assisted reproductive technology due to infertility) with polihidramnios developed a SHiP due to haemorrhage from varicosities on the left lateral surface of the uterus. Bleeding control was difficult and foetal death was confirmed the day after the surgery. Case 2: A 21 week primigravida developed a SHiP originating from bleeding of an accessory posterior branch of the left uterine artery. This was ligated, stopping the haemorrhage immediately. Pregnancy was uneventful thereafter, and a healthy term newborn was delivered. Case 3: A 24 week pregnant woman, *grávida 4, para 2*, developed a SHiP. During surgery, multiple uterine varicosities were identified and the haemorrhage was traced to a varicose vessel at the infundibulopelvic ligament, requiring right adnexectomy for bleeding control. On the following day, she developed a hemoperitoneum again; this time, foetal death was confirmed. Laparotomy with caesarean section was performed for haemostatic purpose. Case 4: An 11 week primigravida with a myomatous uterus developed a SHiP. During laparotomy, the source of bleeding was identified as being a varicose vessel from a 20cm subserous myoma. Myomectomy was performed, resolving the haemorrhage. She delivered a healthy term newborn after a pregnancy without further complications. **Conclusion:** In our series of four cases, there were none of maternal mortality and half had a favourable obstetric outcome. One can see variation in presentation, risk factors, triggering causes, and outcomes. This demonstrates the importance of clinicians being alert to this rare but life-threatening possibility.

P066

INTRA-UTERINE TOTAL RUPTURE OF A VELAMENTOUS UMBILICAL CORD; A CASE REPORT

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Objective: To report a rare case of intrauterine fetal death secondary to spontaneous antepartum rupture of a velamentous umbilical cord. **Study design:** Case report. **Case report:** A 24-year-old healthy woman, G1P0, was admitted to our medical center at 39 weeks of gestation due to reduced fetal movements. No other symptoms were present, including uterine contractions or vaginal bleeding, and no preliminary traumatic events were reported. The pregnancy was conceived by in-vitro fertilization with intracytoplasmic sperm injection, and the antenatal period was uneventful. Ultrasound examination demonstrated intra-uterine fetal death, with no sonographic evidence of placental abruption. Induction of labor was performed by administration of oxytocin and amniotomy. Amniotic fluid was blood-stained. Due to prolonged second stage, and maternal request, a vacuum extraction delivery was performed, with gentle traction and without any complications. A stillborn female was born, weighting 3110 gram, with no signs of extrinsic malformations. Following the delivery a complete rupture of velamentously inserted umbilical cord was observed. The cord

contained three vessels, and the separation occurred close to the velamentous insertion. Pathologic examination demonstrated a third trimester mature placental tissue with areas of infarction, and an umbilical cord with three blood vessels and no signs of inflammation. **Conclusions:** To our knowledge, this is the first reported case in the modern literature, of fetal death related to antepartum total rupture of a velamentous umbilical cord, especially when occurring spontaneously before the onset of contractions or rupture of membranes. Antenatal diagnosis of velamentous insertion is possible with today advanced instrumentation, however, it is not clear if such umbilical cord accidents can be prevented.

P067

PRENATAL DIAGNOSIS OF IDIOPATHIC INFANTILE ARTERIAL CALCIFICATION (IIAC): CASE REPORT AND LITERATURE REVIEW

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Problem statement: Idiopathic infantile arterial calcification (IIAC) is a rare autosomal recessive disease characterised by extensive calcifications of medium and large-sized arteries. Because of the severity of the disease, most cases were detected on prenatal ultrasound (US). **Methods:** 4weeks' gestation developed fetal ascites, hepatosplenomegaly identified on a second trimester US. The placenta was markedly thick with ground-glass appearance. **Results:** An emergency caesarean section was performed at 29 weeks due to disease progression. Despite the aggressive therapy, neonatal death at 2 months of life as a result of multi-system organs failure. Pathological findings were remarkable for fetal chorionic plate vessels mural calcifications in the absence of avascular villi. **Conclusion:** Examination of placenta by imaging and pathology are considered an alternative and valuable tools in IIAC diagnosis.

P068

A THREE-YEAR RETROSPECTIVE STUDY OF AMNIOCENTESIS: IN A DISTRICT HOSPITAL

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Problem Statement: To evaluate the results and complications of amniocentesis procedure for prenatal diagnosis. **Methods:** Retrospective review of clinical charts of all pregnant women had undergone amniocentesis in our department during the period 2015-2017. **Results:** Amniocentesis was performed in 413 pregnant women. Maternal age ranged from 16 to 46 years (mean 37years) and the mean gestation age at amniocentesis was 16weeks+3days. The most common indication was advanced maternal age (over 35 years old) in 60% followed by positive combined screening (16%), increased nuchal translucence (8%), personal/obstetrical or family history of fetal malformations/genetic diseases (6%), other abnormal ultrasound findings (5%), infections (1%) and other reasons (0.24%). Abnormal karyotype was found in 8 out of 248 patients with advanced maternal age (3%), in 8 out of 65 of those with positive screening (12%), in 4 out of 32 of those increased nuchal translucence (12.5%), in 3 of 25 of women with personal or familiar history (12%) and in 2 of 21 of the group with abnormal ultrasound findings (9%). The chromosome results were normal in 93.9% (n=388) of cases and consistent with Down's syndrome in 7 cases, Edward's syndrome in 3, X trisomy in 2, Klinefelter syndrome in 2, Turner syndrome in 1, microdeletion in 2 and others 7. The outcomes of pregnancies were: 379 live births, 3 cases of late miscarriage (2 had abnormal karyotype), 1 stillbirth (34w) and 19 elective terminations (13 due to chromosomal



abnormalities and the remainder due to echographic changes but normal karyotype). We didn't have access to information after invasive procedure in 2,6% of the patients. **Conclusion:** Although advanced maternal age was the main reason for amniocentesis in our sample we concluded that in this group the percentage of abnormal karyotype was only 3% (75% in women over 38 years old). The post amniocentesis rate of fetal loss was less than 1% (0.72%) in our center, with an abnormal karyotype being detected in 0.48% of those cases. Although it may lead to serious complications, this technique is the most commonly and easily performed and reliable test for prenatal diagnosis of genetic diseases.

P069

THE EFFECTS OF PHALERIA MACROCARPA (SCHEFF.) BOERL EXTRACT ON MALONDIALDEHYDE (MDA) LEVEL IN PREECLAMPSIA-INDUCED HUMAN UMBILICAL VEIN ENDOTHELIAL CELL (HUVEC) CULTURE

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Abstract: Preeclampsia is a major cause in both maternal and perinatal mortality and morbidity. The etiopathogenesis of preeclampsia is still not fully elucidated but it is believed to be a multifactor. Endothelial dysfunction plays a big role in the pathophysiology of preeclampsia. Impaired utero-placental perfusion in PE causes hypoxia, ischemia, placental oxidative stress, so the placenta produces free radicals such as superoxide anions (O_2^-) and H_2O_2 , trophoblast debris, pro-inflammatory cytokines, and antiangiogenic factors which are thought to cause vascular endothelial dysfunction and causing excessive maternal inflammatory responses. Oxidative stress is considered as a mediator of endothelial dysfunction in preeclampsia. Pregnancy itself is a state of oxidative stress along with mitochondrial activity and increased production of Reactive oxygen species (ROS) but is offset by increased antioxidants production. Increased oxidative stress and lipid peroxides and reduced antioxidants play a role in the pathophysiology of preeclampsia. Malondialdehyde (MDA) is the final product of lipid peroxidation, thus it is used as one of the oxidative stress marker. In vitro model research is considered the best and most effective way to understand the disease pathophysiology. HUVEC culture is an in vitro model widely used to study the pathogenesis of preeclampsia *Phaleria macrocarpa* (Scheff.) Boerl also known as Mahkota Dewa is widely used as an antioxidant. This study aimed to determine the effects of *Phaleria macrocarpa* (Scheff.) Boerl Extract on MDA Level In preeclampsia-induced HUVEC. **Methods:** The study design is true experimental laboratory post test only with control group using HUVEC ATCC CRL 1730 Cell Line. **Result:** Our results showed the *Phaleria macrocarpa*'s extract reduce MDA level significantly at concentration of 3.906 $\mu\text{g}/\text{mL}$ in preeclampsia-induced HUVEC culture. *Phaleria macrocarpa*'s extract at concentration 15.625 $\mu\text{g}/\text{mL}$ reduce MDA level to control normal level. **Conclusion:** Thus, *Phaleria macrocarpa*'s extract might be used as antioxidant in preeclampsia. Since the decreased the level of MDA in preeclampsia-induced HUVEC culture, further clinical studies regarding the use of *Phaleria macrocarpa*'s extract in treatment are encouraged.

P070

CONGENITAL HIGH AIRWAY OBSTRUCTION SYNDROME (CHAOS) AS PART OF A POLIMARFORMATIVE SYNDROME

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Problem Statement: Congenital high airway obstruction syndrome (CHAOS) is a rare, life-threatening condition in which there is an intrinsic complete or partial obstruction of the fetal upper airway. The most frequent cause is laryngeal atresia. The obstruction of the upper airway leads to entrapment of fetal lung fluid outflow causing increased volume of lungs thereby leading to compression of heart and mediastinal structures. The prenatal ultrasound findings of CHAOS include large echogenic lungs, flattened or inverted diaphragm, dilated airways distal to the obstruction, and fetal ascites and/or hydrops. Although the exact incidence is not known more than 100 cases of CHAOS have been reported and about half of them were complicated with associated anomalies (cardiocirculatory, musculoskeletal, genitourinary and gastrointestinal systems). The most common associated genetic disorder with CHAOS is Fraser's syndrome (urogenital defects, laryngeal atresia, syndactyly and cryptophthalmos). CHAOS was previously equivalent to fetal death. However, there have been some reports of successful intrauterine and ex utero intrapartum treatments especially if an incomplete obstruction is diagnosed in the late 2nd or in the 3rd trimester and if severe hydrops has not occurred yet. **Methods:** Description of a case of CHAOS diagnosed on antenatal ultrasound. **Results:** A 25-year-old pregnant female (gravida 3, para 2) was referred to our institute at 22 weeks due to anomalies in the 2nd trimester ultrasound. Her medical and familial medical history was unremarkable. Ultrasound examination of the fetus in our institute revealed polymarformative fetus with lungs symmetrically enlarged and highly echogenic, trachea dilatation, inverted hemidiaphragm, compressed tubular heart and severe ascites. Furthermore both feet showed altered axis, there was ventriculomegaly, agenesis of the corpus callosum and hypoplastic kidneys. During the ultrasound, it was not possible to visualize the bladder and genitals. Amniocentesis was performed and PCR-aneuploidy was negative for T21/T13/T18. The termination of pregnancy was requested by parents. **Conclusions:** CHAOS is a rare cause of congenital airway obstruction, which is incompatible with life. Antenatal ultrasound can lead early diagnosis of this condition and allow to inform the parents about fetal prognosis.



P071

PROM IN 25-30 WEEKS AND PREGNANCY PROLONGATION. WHAT AFTERBIRTH PROVES?

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Problem statement: Preterm rupture of fetal membranes (PROM) is a complication of pregnancy which foresees preterm delivery after respiratory distress syndrome prophylaxis and prolongation of pregnancy till the development of preterm labor or the signs of chorioamnionitis or fetus distress. **The aim of research:** was improvement the perinatal outcomes of pregnancy in cases of PROM in term of 25-30 weeks and the decrease of neonatal morbidity on the basis of choice of the rational obstetric tactics and of the study of morphological peculiarities of 30 afterbirths from preterm labor with anhydrous period to 48 hours. **Materials of research:** were 30 cases records of preterm labor with PROM finished with alive births and 30 afterbirths, which have evaluated after staining by hematoxylin and eosin. **The methods of research** were clinical, CTG, USG, morphological, statistical methods. **Results:** Inflammatory changes have been found out in 100 % of cases in fetal membranes and in umbilical cord (in 33,33±8,75 % phlebitis, in 10,0±5,57 % arteritis, in 30,0±8,51 % vein dilatation, in 16,67±6,92 % perivascular hemorrhages, in 20,0±7,43 % edema). In placenta fibrin-leukocyte intervillitis in 90,0±5,57 %, basal deciduitis in 56,67±9,2 %, basal decidua infiltration in 13,33±6,31 %, acute placentitis in 33,33±8,75 %, acute villitis in 23,33±7,85 %, acute placental chorioamnionitis in 23,33±7,85 %, villi edema in 23,33±7,85 %, placenta morphological immaturity in 90,0±5,57 %, pseudoinfarctions in 56,67±9,2 %, intervillous space thrombosis in 26,67±8,21 %, villi hypovascularization in 26,67±8,21 %, avascularization in 10,0±5,57 %, villi infarctions in 26,67±8,21 %, vases obliteration in 6,67±4,63 %, subchorial hemorrhages in 13,33±6,31 %, villi stroma fibrosis in 23,33±7,85 %, placenta petrification in 26,67±8,21 % of cases have been found out. Placenta hypovascularization and villi avascularization, villi infarctions and pseudoinfarctions, morphological immaturity of placenta are the morphological markers of placental insufficiency and fetal hypoxia. **Conclusion:** Inflammatory changes, morphological signs of placental insufficiency and fetus hypoxia in afterbirths have been found out. CTG and USG fetal monitoring, immediately delivery in fetal distress are the main methods of perinatal mortality prevention. The question is how to prevent the development and decrease display of fetal hypoxia? The authors declare absence of conflict of interest.

GYNECOLOGY

P072

PATHOGENETIC EFFECTS OF FOLATE-CONTAINING COMBINED ORAL CONTRACEPTIVE IN PATIENTS WITH PCOS

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Problem statement: Hyperhomocysteinemia plays a role in the development of cognitive dysfunction and depression. Along with metabolic disorders, PCOS is known to have negative consequences for the psychological sphere of patients. Such psychosocial disorders as depression, anxiety, dissatisfaction with one's body, episodic bulimia and decreased sexual satisfaction are widespread. These accompanying mental problems affect the quality of patient's life. **Objective:** To study the effects of folate-containing combined oral contraceptive (COC) with drospirenone on hyperandrogenism and the severity of anxiety and depression in patients with PCOS compared to COC without folate. **Methods:**

questionnaire based on the hospital scale of anxiety and depression (HADS), anthropometric measurements (body mass index (BMI), waist / hip circumference), evaluation of the severity of hirsutism on the Ferriman-Hallway scale, the examination of the concentration of testosterone and insulin in blood serum initially and after 3 months of observation. Patients. 85 patients with PCOS at the age of 17-35 years. Interventions: 30 women received a COC containing 3 mg of drospirenone, 30 µg of ethinyl estradiol and 451 µg of calcium levomefolate (1 group), 30 women received a COC containing 3 mg of drospirenone and 30 µg of ethinylestradiol (2 group), 25 patients did not receive a therapy (3 group). **Results:** After 3 months of therapy a statistically significant decrease in testosterone and hirsut-number in the groups of patients receiving COC was observed in comparison with the initial parameter (p<0.05). Metabolic profile of patients (BMI, waist / hip circumference and insulin level) of all groups did not change in the background of 3 months of follow-up. All patients showed signs of anxiety and / or depression initially, after 3 months of treatment in the folate-containing contraceptive group, signs of anxiety and / or depression were almost completely stopped (p<0.05), in the 2nd group the borderline state of patients remained. **Conclusion:** Adding an active form of folic acid to COC can increase the effectiveness of treatment of patients with PCOS and severe psycho-emotional disorders.

P073

PARATUBAL CYSTS: A RARE CAUSE OF ADNEXIAL TORSIO

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Problem statement: Paratubal cysts, also known as paraovarian cysts or hydatid of Morgagni, represent approximately 10% of all adnexal masses and are believed to originate from the mesothelium or to be remnant of paramesonephric or mesonephric ducts. Small paratubal cysts are mostly common between 30 to 40 years and are often indistinguishable from simple ovarian cysts. Ultrasound scan is the first line exam, whereas magnetic nuclear resonance is useful to clarify the diagnosis. A paratubal cyst is often connected with the mesosalpinx by a stalk, in which torsion rarely occurs, sometimes involving the tube, thus causing acute severe pain requiring emergent surgical intervention. **Methods:** We report a case of a paratubal cyst torsion with involvement of the tube, treated by complete laparoscopic enucleation. **Results:** A 36-year-old woman, one previous c-section, without other relevant antecedents, presented at our urgency department with gradually increasing right iliac fossa pain in the previous 4 days accompanied with nausea and vomiting. A similar episode occurred two months before. There was no anorexia, weight loss or weakness and bladder function was normal. She had regular menstruations and she affirmed using a barrier method consistently. At abdominal examination, there was no significative pain. Through vaginal bimanual examination in Douglas cul-de-sac, a very painful elastic mass was palpated at right. Blood tests showed no infectious parameters, B-HCG and urinalysis were negative. Ultrasound scanning next to right ovary showed a homogeneous anechoic cyst with thin walls that showed hemorrhagic components measuring 42 x 49 mm, confirmed by computed tomography, which excluded appendicitis. Paratubal cyst or hydrosalpinx were suspected and diagnostic laparoscopy was proposed. A right paratubal cyst was observed which was causing fallopian tube torsion. After tubal torsion removal, the patient underwent cystectomy without rupture, neither compromise of the ovary or fallopian tube. Histologic examination revealed a hydatid cyst of Morgagni with hemorrhagic alterations. The admission was otherwise uneventful, with discharge at day 2. **Conclusion:** Although twisted paratubal cyst is rare, it should be kept as differential diagnosis in any patient presenting with acute or intermittent pelvic pain who has a paratubal cyst identified on pelvic ultrasound.

P074

MALIGNANT PHYLLODES BREAST TUMOR IN A 16-YEAR-OLD GIRL: A CASE REPORT AND REVIEW

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Problem statement: Phyllodes tumor (PT) of the breast is a rare fibroepithelial neoplasm, accounting for 0.3% to 0.9% of all breast tumors (mean age 40 years). Clinical presentation consists in a mobile, non-painful, rapidly enlarging breast lump with great predisposition to recurrence. **Methods:** We report a 16-year-old girl followed in our Breast Unit, who had previously undergone 6cm-left breast adenocarcinoma excision. She reconsults 15 months later, due to reappearance of a 3-4cm left retro-areolar lump. The ultrasound revealed a 26x15x21mm solid lump with heterogeneous echo pattern, areas of cystic degeneration and increased vascularity, which led to suspicion of adenocarcinoma recurrence (BIRADS 4a). A biopsy was performed and the anatomopathologic examination showed a fibroepithelial lesion with an increased mitotic activity, classifying the tumor as borderline/malignant PT. A tumorectomy was performed with a final diagnosis of malignant 34x30mm PT with positive resection margins. Finally, a left mastectomy with periareolar access (including recent tumorectomy scar) was done. Immediate breast reconstruction was performed and a 295-cc polyurethane prepectoral implant covered with an acellular dermal matrix was placed. Two surgical drains were left. Anatomopathology study did not show features of malignancy and today she remains disease-free. **Results:** Hystological characteristics are the basis for diagnosis of PT but mammography and ultrasound are useful for its identification. The recommended treatment is complete surgical excision (mastectomy if necessary) with 1 cm margins. Radiation treatment can be an option in selected patients but its use is controversial. The use of routine hormone therapy or chemotherapy is not encouraged. **Conclusion:** Malignant PT is an extremely rare neoplasm that makes its diagnosis and treatment a challenge due to its clinical presentation, rapid evolution and high recurrences rates.

P075

PREVALENCE OF URINARY INCONTINENCE IN AN OBSTETRICS AND GYNECOLOGY PRIMARY CARE OF BARCELONA

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Problem statement: To determine the prevalence of urinary incontinence (UI) in an obstetrics and gynecology Primary Care Center of our area of influence at the University Hospital del Mar, Barcelona. **Methods:** A cross-sectional study was performed. All women attending general gynecology consultation during a 5 period of 5 months (from August 2017 to January 2018) were included, regardless the reason for such consultation. To assess UI, the Spanish version of the "International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form" (ICIQ-SF) was used. The degree of quality of life alteration was assessed by the analogue scale included in the test (1 to 10). Chi-square (X²) and Fisher's exact test were performed for the analysis of categorical variables. Statistical analysis was performed with SPSS v22. **Results:** 450 women were enrolled, with ages between 16 to 89 years (mean 40.7 years). 43.3% of the patients presented any grade of UI. The prevalence of UI in the different age groups was 6.2% (in the group of 16 to 25 years), 42.1% (from 26 to 45

years), 40.5% (from 46 to 65 years), 7.2% (from 66 to 75 years) and 4.1% (75 years). Considering the parity status, the prevalence of UI was 15.4% in nullipara, 26.2% in primipara, 42.1% in women with 2 births and 16.4% in women with 3 or more births (p values 0.05). The results of the ICIQ-SF assessed on the 43.3% of patients affected with UI showed that, in 7.3% it was severe, in 7.8% it was moderate, and in 22.9% it was mild. Paradoxically, 5.3% of urinary incontinent patients scored 0 points in ICIQ-SF. Quality of life (QOL) was importantly altered in all patients with a severe degree of UI. **Conclusion:** Prevalence of UI in the studied area has been found to be 43.3%, but it's noteworthy that only 5.5 % of them consulted for pelvic floor dysfunction, constituting a small cohort.

- UI is a prevalent health problem which is not often a reason of consultation.

- Alteration in the quality of life may be the instigator factor for the patient to ask for help.

P076

POTENTIAL ROLES OF AQUAPORIN 9 IN THE PATHOGENESIS OF ENDOMETRIOSIS

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Problem statement: Considering the fact that chronic inflammatory processes and increased potentials of cell invasion, migration, and proliferation are pivotal processes involved in the pathogenesis of endometriosis, we hypothesized that AQP9s are differentially expressed in the endometrium of the patients with endometriosis than those without the disease. In this study, we evaluated expressions of AQP1-9 in patients with and without endometriosis and investigated whether modulation of specific AQP9s is involved in the pathogenesis of endometriosis. **Methods:** Expressions of AQP subtypes in eutopic and ectopic endometrium of patients with and without endometriosis were evaluated using the NanoString nCounter System and western blotting. The HESCs were cultured and transfected with the siRNA of the AQP9 of interest. Expressions of AQP9 subtypes were compared between the group with endometriosis and the group without the disease. After siRNA transfection of AQP9 subtypes of interest into HESCs, migration and invasion potentials and expressions of matrix metalloproteinase 2 (MMP2), MMP9, extracellular signal-regulated kinase 1/2 (ERK 1/2), and p38 mitogen-activated protein kinases (p38 MAPK) were evaluated. **Results:** Among the AQP1-9 subtypes, endometrial expression of AQP2 and AQP8 was significantly increased, whereas AQP9 expression was significantly decreased in the Eu-EMS group compared to the Eu-CTL group. Comparison of expression of AQP2, AQP8, and AQP9 among Eu-EMS, Ect-EMS, and Eu-CTL groups revealed significant differences for only AQP9. Expression of AQP9 in the Eu-EMS group was decreased compared with those of Eu-CTL. After transfection of AQP9 siRNA in HESCs, expression of MMP2 and MMP9 were significantly elevated. Increased expression of phosphorylated ERK 1/2 (p-ERK 1/2) and phosphorylated p38 MAPK (p-p38 MAPK) proteins after transfection was also confirmed using western blot analysis. Increased migration and invasion potentials of HESCs after transfection were determined by migration and wound healing assays. **Conclusion:** Several AQP9 subtypes were aberrantly expressed in endometriosis, and down-regulation of AQP9 in HESCs significantly increased migration and invasion potential through modulation of MMP2 and MMP9 and involvement of the ERK/p38 MAPK signaling pathway. These findings suggest that AQP9 may be involved in the pathogenesis of endometriosis and imply the potential that AQP9 could be a therapeutic target for treating endometriosis.



P077

PERSONALISED ALGORITHM IN PATIENTS WITH MYOMA UTERI AFTER MYOMECTOMY BASED ON EPIGENETIC DETERMINANTS
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The risk concept of operative treatment of fibroids based on epigenetic determinants, clinical evidence, anaemnesis, menstrual disorders, gynecological diseases, extragenital pathology, ultrasound data, immunohistochemistry and histological examinations of nodes are developed in this study. The samples were obtained during the conservative myomectomy or hysterectomy in 158 patients aged 32 to 45 years. The control group included samples of biopsies of normal myometrium taken from the same patients. The status of DNA methylation of genes ESR1 α , PgR-Band WIF1 have been examined in myoma nodes of 60 patients. Isolation of DNA:the received tissue samples were grounded into pieces to 2 g, which are then lysed in order to isolate and transfer the DNA unmethylated cytosine residues to thymine while maintaining unchanged methylated cytosine residues. Then PCR have been performed. Sequencing was carried out in the center of collective use "Gene" at the Institute of Molecular Biology of V.A. Engelhardt RAS based on standard protocol using forward primers and kit reagents ABI PRISM® BigDye™ Terminator v. 3.1. The standard methods of ultrasound diagnostics, immunohistochemistry and histological examinations have been used in all patients. We have prepared computerized programme based on Microsoft Office Excel for analyzing the risk of development of progressive course of myoma uteri of every patient. The 3 groups of women have been formed based on likelihood of developing of rapid growth of fibroids: low (p0,29), moderate (0,29

P078

COMPARATIVE STUDY OF SKIN CLOSURE METHODS OF HUMANISED MICE SKIN SAMPLES
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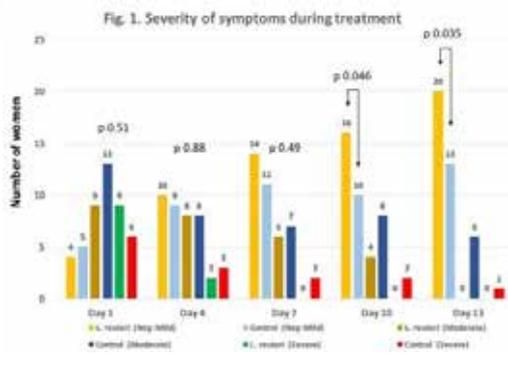
Objective: Operative wound closure with good cosmetic outcome is paramount to surgeons as testimonial to their surgical finesse. Many studies have compared clinical cosmetic outcomes of suture and tissue adhesive skin closure in humans and rats. However, rat studies are flawed as they lack the human immune response to wound healing. We aim to use humanised mice with a stable human immune system to compare wound healing of skin closure of humanised mice skin samples with healing by secondary intention, suture closure, suture closure with sub-dermal steroid injections, as well as skin adhesives. **Methods:** Humanised mice models were prepared using human fetal liver stem cells via intracardiac injection into one-day old mouse pups. Twenty humanised mice were divided into 4 groups of five mice each. A 2-cm transverse incision made on the mouse abdomen was closed with the following methods: secondary intention, suture closure, suture closure with sub-dermal steroid injections, and tissue adhesive Dermabond™. The wounds were reviewed on the 3rd, 7th, 14th and 21st post-operative days. The histopathology on post operative day 21 evaluated the following aspects: granulation tissue, acute inflammatory exudates, foreign body giant cell reaction, re-epithelialisation, squamous hyperplasia, dermal fibrosis and keloid formation. **Results:** All wounds had good recovery by the 21st operative day. With regards to histopathology, suture with sub-dermal steroid injection had the most cases of poor re-epithelialisation and acute inflammatory exudates at day 21, with

one case of abscess formation. Dermabond™ had the least foreign body giant cell reaction, with moderate granulation tissue formation and one case of failure of epidermal recovery. Suture skin closure has the best cosmetic and histological appearance. **Conclusion:** These results show that all methods of skin closure will eventually lead to skin recovery. However, the amount of inflammatory response may influence the cosmetic appearance. Given the humanised immune response in the humanised mice, we postulate that these results can be extrapolated to human skin wound healing for surgical consideration. Conventional suture skin closure remains the best option.

P079

EFFICACY OF LACTOBACILLUS REUTERI STRAINS DSM 16666 AND DSM 17938 FOR TREATMENT OF URINARY TRACT INFECTIONS IN PREMENOPAUSAL WOMEN: A PROOF-OF-CONCEPT RCT
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Problem Statement. Urinary tract infections (UTIs) are the most common bacterial infection in women, with approximately 50% of women experiencing at least one UTI in their lifetime. Probiotics have been considered to be an alternative to antibiotic use. The aim of this Proof of Concept was to assess the effectiveness of *Lactobacillus reuteri* strains DSM 16666 and DSM 17938 in combination with cranberry PAC (proanthocyanidins) and zinc for the treatment of acute non-complicated urinary tract infections in premenopausal women. **Methods.** Premenopausal women with acute non-complicated UTI and attending an ambulatory center were enrolled in this randomized, double-blind, placebo-controlled trial. Subjects received orally 2*10⁸ CFU of *Lactobacillus reuteri* strain DSM 16666 and 1*10⁸ CFU of *Lactobacillus reuteri* strain DSM 17938 in combination with cranberry PAC and zinc (n=22) or placebo (n=24) two times daily for 12 days, after which they were followed up for 18 days without treatment. **Results.** At the end of treatment, the clinical cure was significantly better in the group who received the product with probiotics, PAC and zinc. The percentage of women with negative to mild severity of symptoms was 91% in the active group vs. 54% in the placebo group (p0.05) (Fig. 1). Additionally, the number of women with moderate number of urinary leukocytes was more reduced in the group receiving probiotics, PAC and Zn compared with the control group, (31% vs 4 %). The frequency of adverse events was similar in both groups. **Conclusions.** This study supports the use of *Lactobacillus reuteri* strains DSM 16666 and DSM 17938 in combination with PAC and zinc as an effective and safe therapeutic alternative for the treatment of uncomplicated UTI in premenopausal women. *Trial registration.* ClinicalTrials.gov ID: NCT03019172. Disclosure of interest: Authors declare any conflict of interests



P080

MANUAL VACUUM ASPIRATION IN SURGERY FOR MISCARRIAGE IN EARLY PREGNANCY FROM A STANDPOINT OF ENDOMETRIAL PROTECTION

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Problem statement: Dilatation and curettage (D&C) is generally performed for surgical treatment of miscarriage in early pregnancy in Japan, but aspiration is mainly performed in other countries. This is because D&C is a possible cause of endometrial thinning and Asherman syndrome. Manual vacuum aspiration (MVA) became common in the 1990s in Western countries. In Japan, a MVA device (the MVA kit) was approved in October 2015, and our hospital started using MVA alone for surgical treatment of miscarriage in early pregnancy in June 2016. In this study, we investigated the usefulness of the MVA kit for this purpose.

Methods: The subjects were 338 patients who underwent surgery for miscarriage at earlier than 12 weeks of gestation at our hospital between January 2014 and June 2018 and gave informed consent. Among these patients, 121 were treated with D&C, 108 were treated with electric vacuum aspiration (EVA) alone, and 109 were treated with MVA alone. Operative time, blood loss, amount of anesthetics used, presence of remnants and reoperation, and complications were investigated in each group. Endometrial thickness was investigated before and after surgery in the MVA group, using the mean in several cycles from ovulation to implantation. Endometrial thinning was defined as an endometrial thickness 7.0 mm in the ovulation phase on transvaginal sonography. **Results:** The mean ages of the D&C, EVA, and MVA groups were 33.8, 34.0, and 34.7 years old, respectively. Blood loss ≥ 100 mL occurred in 3 patients in the D&C group, but in no patients in the EVA and MVA groups. There were no significant differences in operative times and anesthetics used among the groups. Remnants of uterine content were noted in 3, 2, and 1 patients in the D&C, EVA, and MVA groups, respectively. Endometrial thickness did not change after surgery for miscarriage in the MVA group. The incidence of endometrial thinning was significantly higher in patients with a history of curettage for miscarriage in our hospital. No severe intra- or postoperative complications developed in any patients. **Conclusion:** These results suggest that a MVA kit for surgery for miscarriage is useful from the standpoint of endometrial protection.

P081

THE ROLE OF GENETIC FACTORS IN THE CYTOKINE PROFILE IN THE DEVELOPMENT OF ENDOMETRIAL HYPERPLASIA PROCESSES IN PERI- AND POST-MENOPAUSE

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Imbalance of factors of proliferation and apoptosis in conditions of progesterone and estrogen deficiency in women in peri- and postmenopause leads to the development of endometrial hyperplasia (EH). However, if hormonal imbalance is inherent in all women of this age, the development of endometrial pathology, mainly manifested by dysfunctional uterine bleeding (DUB), occurs in a certain group of women. The search for genetic markers that explain the pathogenesis of EH will help to conduct a personalized approach to the prevention and therapy of these conditions. 35 women with EH, showing clinically uterine bleeding (the main group) were examined. The control group consisted of 43 conditionally healthy women. All women in the main group underwent endometrial biopsy and subsequently histological diagnosed: simple hyperplasia without atypia in 17 (48.6%), complicated without atypia in 10 (28.6%), atypical EH in 8 (22.9%) patients. A genetic study was carried out by isolating DNA and determining in the blood serum the functionally unfavorable genotypes (G/A) of Tp-53 tumor growth suppressor genes and the pro-inflammatory cytokine TNF- α . Analysis of the polymorphism rs1800629 evaluation of the TNF- α gene in the development of EH showed that the genetic marker G-380-A was significantly more reliably detected in the G / A genotype in 18 (51.4%) women, $P = 0.002$, $\lambda^2 = 9.3$, $RR = 2.8$, $OR = 4.6$, (95% CI 1.68- 12.78), compared with the control group in 8 (18.6%), which indicates a statistically significant result. While the determination of the genotypes of the polymorphism of the Tp-53 gene showed a less pronounced difference in the determination of the heterogeneous genotype Arg / Pro (-/+) in women with EH - in 18 (51.4%) compared to the control group - in 16 (37.2%), ($OR = 1/9$), which indicates a trend towards the development of EH with this variant of the genotype of this marker. The gene-gene interaction of the detectable markers showed that the combination of the genotype G / A (-/+) genotype of TNF- α and Arg / Pro (-/+), the Tp-53 gene, unfavorable for DUB development, was detected in 7 (20%) women with DUB and 3 (6.9%) - in healthy women.

P082

ANGIOMYOFIBROBLASTOMA OF THE VAGINA WHICH MIMICS AGGRESSIVE ANGIOMYXOMA

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Problem statement: There are various types of Vaginal mass and the most common type include Bartholin cysts, Gartner's duct cyst, vaginal inclusion cyst. Meanwhile Angiomyofibroblastoma is a rare tumor which is benign but significant consideration in differential diagnosis with Aggressive angiomyxoma. **Methods:** We report a case of angiomyofibroblastoma arising from Vagina in pre-menopausal woman concentrating upon the fact that this type of tumor can arise from the vagina. **Results:** It was firm like a fibroid in consistency so this initially mimicked intraligamentary myoma or protruding subserosal myoma. vaginal mass excision was done with clear resection margin. **Conclusion:** Histogenesis of angiomyofibroblastoma is not clearly known, but it may show similar morphological, cytogenetical, immunohistologic features with Cellular angiofibroma and aggressive angiomyxoma. Thus, Differential diagnosis is essential.

P083
EFFECTIVENESS OF ULTRASOUND-GUIDED ASPIRATION AND ETHANOL SCLEROTHERAPY FOR TREATMENT OF ENDOMETRIOMA

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Problem statement: To evaluate the effectiveness of ultrasound-guided aspiration and ethanol sclerotherapy for treatment of endometrioma. **Methods:** From May 2017 to August 2017, 28 patients (age range 24~43 years) with endometrioma (2.9-9.7cm) underwent ethanol sclerotherapy. We performed aspiration using 20cm, 18 gauge needle. After aspiration about forty percent of aspirated fluid was replaced with 95% ethanol, which was left in situ for 5min, 2times total 10min. Clinical follow up(median follow up, 12 months) was performed for all the patients.

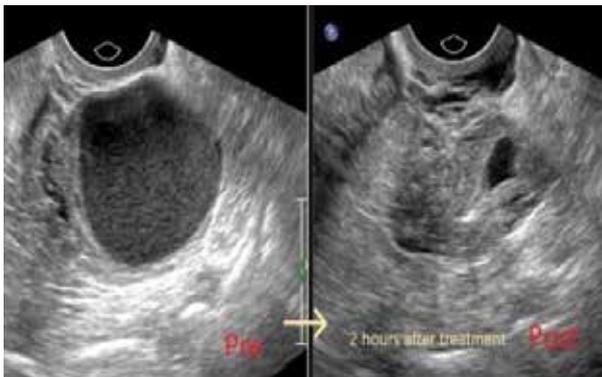


Fig1. Ultrasound image.

Results: The procedure was successful in all patients. The 1-year recurrence rate after sclerotherapy was 1 case (3.6%). there were no major complication, malignant cells were not found in all cases at cytologic examination. **Conclusions:** Ultrasound-guided aspiration and ethanol sclerotherapy is an effective and safe treatment for ovarian endometrioma.

P084
REPRODUCTIVE SURGERY OF UTERINE ANOMALIES USING FUNCTIONAL MRI

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Problem statement: Successful reproductive outcomes of patients with uterovaginal anomalies reach up to 25-37%, despite applying the minimally invasive surgical corrections and assisted reproductive methods (IVF). Optimistic reproductive prognosis in some patients with uterine maldevelopment depends on the anatomy and uterine blood supply. **Methods:** Between 2015 - 2017 were examined 213 patients with symmetric uterine anomalies. For estimation of myometrial blood perfusion parameters involved the new method of functional or dynamic contrast enhanced MRI, using the intravenous injection of gadolinium. The functional MRI was performed for 42 patients requiring surgery and for 30 patients managed without surgical correction. **Results:** Dynamic monitoring of serial images evaluates the blood perfusion by digital diagram and color – mapping. Clinical analysis of reproductive outcomes before and after surgery correlatively with data of DCE MRI of women with uterine anomalies. According to the DCE MRI parameters, patients with intrauterine septum were identified into 2 groups: 1) patients with normal blood perfusion in the septum, which are in 86% cases had successful pregnancies; 2) patients with reduced blood perfusion in the septum up to $\geq 20\%$

(comparatively with myometrium), which are in 84% cases had reproductive losses (p0.01). The asymmetric perfusion of duplicated uterus was detected in 85% patients by functional MRI. Successful pregnancy progressed in the hemiuteri with better parameters of blood perfusion (p0.001). These data's correlate with parameters of vascularization and flow capacity in the intrauterine septum by histological morphometry (p0,05). Histological investigations of the resected intrauterine septum indicate: the disorders of blood perfusion caused by severe uterine dysmorphogenesis, vascular malformations and deep myometrial fibrosis. **Conclusion:** Reproductive surgery of uterine anomalies depended on blood perfusion parameters attending to create normally shaped uterine cavity and to eliminate the areas with disturbed blood perfusion, preventing reproductive losses. The functional MRI in patients with duplicated uterus by allows estimating the hemiuteri with better blood perfusion parameters, which is important for embryo transfer in IVF program.

P085
TYPE 3 UTERINE MYOMA WITH NICHE AFTER 3 YEARS FROM UTERINE ARTERY EMBOLISATION

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Problem statement: Uterine artery embolisation is a minimally invasive procedure, using an X-ray camera to guide a specialist, usually an interventional radiologist, to insert a catheter through the uterine arteries and release the embolising agent (polyvinyl alcohol). By reducing the uterine blood flow the fibroid loses 50-80% from its volume in the first 6 months. **Methods:** UAE is not recommended in submucous myomas, reinterventions being frequently in this situation. Secondary hysterectomy is being performed in 13-24% of the cases in the first 2 years and up to 28% of the cases in the first 5 years from the embolisation. The 41-year old patient PM presents 3 years after an UAE with repeated metrorrhagia and pain in the lower abdomen. Ultrasound reveals a tumour on the posterior uterine wall with a 10 cm diameter, tangent to the uterine cavity. Hysteroscopy is being performed to evaluate the extent to the endometrium. The initially obtained image is not clear and it was only later demonstrated that the hysteroscope entered the myoma, this being of a submucous type. **Results and Conclusion:** The patient is being admitted for surgery and myomectomy of a necrotised submucous fibroid of 10 cm is being performed. Evolution of the case is favorable. Ultrasound 6 weeks after surgery reveals a normal-sized uterus with the endometrium in proliferative phase.

P086
THE ROLE OF HYSTEROSCOPY IN THE DIAGNOSIS OF ENDOMETRIAL CANCER

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Problem statement: Uterine cancer is the most common gynecologic malignancy in developed countries. Endometrial carcinoma typically presents with abnormal uterine bleeding and is most common in women who are postmenopausal. Endometrial sampling is the gold standard for evaluation for endometrial neoplasia. Hysteroscopy allows direct visualization of the uterine cavity and endometrial sampling or removal of the lesion during the same procedure. The aim of this study is to evaluate the accuracy of hysteroscopy in the diagnosis of endometrial cancer. **Methods:** retrospective analysis of 515 women (April 2017 to May 2018)



submitted to hysteroscopic and histological evaluation in Centro Hospitalar de Leiria. **Results:** 14 patients were diagnosed with endometrial cancer with the histologic study, 12 of them suspected on hysteroscopy (85.7%). The mean age was 71.6, being 92.8% of the patients postmenopausal. The most common symptom was postmenopausal bleeding present in 85.7% of the postmenopausal patients. All the patients had abnormal findings in the transvaginal sonography. The sensibility and specificity in the hysteroscopic detection of endometrial malignancy were 85.7% and 99% (PPV 70.6% and PNV 99.6%), respectively. **Conclusion:** Although histologic study is mandatory, hysteroscopy seems to be an accurate method in diagnosing endometrial cancer.

P087

THE VALUE OF HYSTEROSCOPY IN POSTMENOPAUSAL WOMEN WITH INCREASED ENDOMETRIAL THICKNESS

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Problem statement: Endometrial carcinoma typically presents with abnormal uterine bleeding and is most common in women who are postmenopausal. Transvaginal sonography is the first step to rule out malignancy. Endometrial thickness more than 4-5 mm in symptomatic women requires additional evaluation. The aim of this study is to assess the role and accuracy of hysteroscopy in postmenopausal women with thickened endometrium. **Methods:** retrospective study of 249 postmenopausal women with transvaginal sonography abnormalities (April 2017 to May 2018) submitted to hysteroscopic and histological evaluation. The cut-off value for endometrial thickness was 4 mm. They were divided in symptomatic (group A) and asymptomatic (group B). Hysteroscopic and histological findings were classified as: normal, benign pathology and malignant pathology. **Results:** Mean age was 65.9 years in group A and 65.7 years in group B. In group A, the hysteroscopy findings suggested benign pathology in 69.9% and suspected malignancy in 16.4%. In group B, the incidence of benign pathology was 88.2% and of suspected malignancy was 1.8%. According to the histological findings, the hysteroscopic diagnosis showed a sensitivity of 95.8%, a specificity of 64.2%, a positive predictive value of 95.3% and a negative predictive value of 66.6%. **Conclusion:** Increased endometrial thickness in postmenopausal women is mostly due to benign lesions. Malignancy is less frequent in asymptomatic women. Although there is no agreement in endometrial thickness for endometrial screening in asymptomatic women, hysteroscopy is a reliable method for evaluation and treatment in both groups.

P088

VAGINAL HYSTERECTOMY IN PATIENTS WITHOUT GENITAL PROLAPSE AND A DEFICIENT CERVIX

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Problem statement: Vaginal hysterectomy should be the approach for hysterectomy whenever feasible. Cervix flush with vagina is considered a contraindication to the vaginal approach. We look at our experience in this group of patients.

Methods: We identified patients without genital prolapse undergoing vaginal hysterectomy and with a possible deficient cervix in our department from 1997 to 2016. The records of these patients were reviewed to identify patients with documented deficient cervix. Information on the operation and postoperative outcome were extracted for analysis. **Results:** Out of 288 patients without genital prolapse undergoing vaginal hysterectomy, 32 patients were considered to have possible deficient cervix. After

review of the medical records, 22 patients were confirmed to have deficient cervix. All hysterectomies were completed vaginally except for one patient who had laparoscopic assistance because of adhesion. In 12 patients, bilateral salpingo-oophorectomies were also performed. All except one had the bilateral salpingo-oophorectomy also completed vaginally. The median operating time was 67 minutes (range: 42-153). Median intraoperative blood loss was 100 ml (range: 20-700 ml). None of the patients were transfused because of blood loss. The patient with 700 ml blood loss was the patient with adhesion requiring laparoscopic assistance to complete the hysterectomy. There were two postoperative complications including one retention of urine and one infected pelvic haematoma. Median hospital stay was 2 days (range: 1-3). **Conclusion:** Vaginal hysterectomy is feasible in patient without genital prolapse and a deficient uterine cervix. Reference: Sheth SS. Preoperative assessment. In: Sheth SS, Studd J, eds. Vaginal hysterectomy. London: Martin Dunitz 2002.

P089

KNOWLEDGE OF PELVIC FLOOR DISORDER IN PREGNANCY

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Problem statement: Pelvic floor dysfunction is common in women. It can lead to distressing consequences such as urinary incontinence (UI), pelvic organ prolapse (POP) and fecal incontinence (FI) with adverse effects on the quality of life of women world-wide. Pregnancy is a known major risk factor for pelvic floor dysfunction. Yet women may not be clearly informed on the importance of maintenance of pelvic floor during pregnancy as a prevention for future pelvic floor dysfunction. This study aims to assess the level of knowledge of pelvic floor disorders amongst pregnant women in our local population, so as to enforce preventive measures in this targeted group. **Methods:** A cross-sectional study was conducted in a population of pregnant women in their third trimester. A questionnaire of 47-questions was distributed to a random sample group. Of which, 11 questions were on demographic characteristics, 8 on obstetric history and current pregnancy, 4 on personal history of pelvic floor dysfunction and 24 on knowledge of pelvic floor disorders. Knowledge scores were calculated. Possible predictive factors for knowledge level such as age, race, parity, ethnicity and educational levels were studied. **Results:** A total of 104 completed surveys were collected. 31.7% respondents reported history of urinary incontinence, 2.9% reported sensation of prolapse and 1 respondent (0.96%) reported fecal incontinence. The knowledge score for urinary incontinence was the highest at 46.2%, followed by fecal incontinence - 39.8% and lowest in pelvic organ prolapse at 35.3%. Respondents who were employed had significant higher mean knowledge scores than those unemployed. Mean knowledge scores increased significantly with age and educational level. The nulliparous women scored higher than the multiparous women. Chinese respondents had the highest mean score. Age and educational level showed significant impact on scores on multivariate analysis. **Conclusion:** Local pregnant ladies are not well informed on the effect of pelvic floor disorders as a result of pregnancy. This is consistent with similar studies worldwide. Emphasis should be placed on pelvic floor exercises during routine antenatal care. This could be achieved through adequate counseling, and the use of interactive pregnancy applications to prevent long term pelvic floor complications in women.



P090

COMPARISON OF TREATMENT REGIMENS OF TUBO-OVARIAN ABSCESSSES (TOA)

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Problem Statement: Fifty per cent of tubo-ovarian abscesses (TOA) are associated with pelvic inflammatory disease. Although antibiotics are the first-line treatment, many patients require surgical or image-guided (IR) drainage. There are no specific factors that can prognosticate the success of either treatment. Our study aims to (i) analyse the demographics of patients with TOA, (ii) identify clinical factors that facilitate treatment decisions, and (iii) compare the outcomes of each treatment regimen. **Methods:** This is a retrospective analysis on patients who were admitted to KK Hospital, a tertiary women's hospital in Singapore from June 2016 to June 2017, with radiological or surgically confirmed TOA. Pregnant patients or patients who were discharged or declined admission against medical advice were excluded. **Results:** A total of 124 patients were recruited and most patients presented with abdominal pain and fever. Of which, 109 (87.9%) patients had antibiotics only, 13 (10.5%) patients underwent IR drainage and 2 (1.6%) patients underwent surgery as initial treatment. Subsequently, 15 (12.1%) patients had IR drainage and 3 (2.4%) underwent further surgery. With larger abscess collection, the odds that the patient requires IR/surgical drainage increased by 1.2 fold (95% CI 1.014-1.440). Patients who had drainage/surgery had a longer intervention to discharge interval, by 1.3 days (95% CI 0.371-2.295), compared to patients who had antibiotics only. They had a significant longer length of stay by 4.6 days (95% CI 3.426-5.690). For patient who requires drainage, a day delay in drainage increases the length of stay by 0.9 days (95% CI: 0.233-1.554); febrile duration by 0.9 days (95% CI 0.388-1.405); duration of intravenous antibiotics by 0.8 days (95% CI 0.332-1.251); and duration of hospitalisation leave by 2.0 days (95% CI 0.511-3.585). **Conclusion:** The size of TOA collection was a significant factor for treatment choice. Drainage by IR or surgery was associated with a longer intervention to discharge interval and length of stay. Early drainage should be done as delay may have adverse outcomes.

P091

DEVELOPMENT OF TRAINING TECHNIQUES IN GYNAECOLOGICAL ENDOSCOPY

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Background: Endoscopy has improved in safety and utility over the years and is now part of standard Gynecological management. But Endoscopy has a learning curve, and this may be steep in some instances. The role of systematic training is to improve the safety and efficacy of surgery and patient outcome. **Problem Question:** Does Endoscopic training match the expectations of patients, trainees and trainers, and is it currently being done in a systematic, safe, graded and effective manner with adequate supervision? **Study design:** Comparative analysis of training in Gynecological Endoscopy in different parts of the world. This study compared and contrasted various centres in different countries worldwide, along with surveys of users and a review of literature in the field. **Materials & methods:** Trainees and trainers in Gynecological Endoscopy in various centres around the world. The survey attempts to identify the strengths and deficiencies of

different methods of training and suggest ways to improve the different techniques. This, we hope will lead to robust discussion and improvement in the way things are done so that future surgeons and patients are benefitted. **Results:** Trainees worldwide have recognized the role of Endoscopy in their future & are extremely keen to develop skills during their training. While some centers have an excellent & structured training, many don't, and there don't seem to be well-defined standards worldwide (or even within the same country in many cases) which trainees should aim to achieve. Limited resources, time, opportunities and supervisors were flagged as important barriers to training as was commitment and communication. Limitations: Limited snapshot from a few centres worldwide. **Implications for our future:** While very limited in the number of centres assessed this study shows the pros and cons of various training methods used in various centres, trainee expectations, and feedback and insights into ways to improve training worldwide. There is an urgent need for improving opportunities for training in this exciting and fast developing field while also maintaining standards and supervision to ensure the safety of patients and the development of good practitioners for the future.

P092

INHIBITORY EFFECT OF TRADITIONAL KOREAN MEDICINE ON THE RECURRENT ENDOMETRIOSIS AFTER LAPAROSCOPIC EXCISION

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Problem statement: Endometriosis is a common benign gynecologic tumor, and it can destroy a patient's life. Surgery and hormone therapy are established therapies for endometriosis. However, there are many cases of recurrent endometriosis after conventional therapies. This report presents a case of a patient who has repetitive recurrence of endometriosis after laparoscopic excision and hormone therapy. **Methods:** A 32-years-old female patient first had laparoscopic surgery to remove endometriosis in 2011. The disease recurred two more times after the first excision. Hormone therapy by dienogest and two more laparoscopic surgeries were done in 2012 and 2014. The patient was prescribed with Traditional Korean Medicine (TKM); acupuncture, moxibustion, fumigation therapy, and herbal medicine therapy (Fig. 1). The acupoints used for acupuncture were CV04, CV06, ST28, EX-CA1, SP06, ST36, SP09 and GV20. Acupuncture was administered for a total of ten sessions during the treatment period, each session lasting twenty minutes. Moxibustion was administered 10 times for 20 min on the lower abdomen using the red clay moxibustion method. The fumigation therapy was done a total of five times using Cnidii Fructus for 20 min during each session. Herbal medicine was prescribed 27 times during the treatment period. The herbal medicines are Boheotang-gagam and Hwa-uh-san according to symptoms.



Results: Endometriosis didn't recur during treatment and observation period of 34 months. Menstrual pain numeric rating scales (NRS) decreased from 2 to none. Shortened menstrual cycle (24 days) after second surgery became longer (26.63 ± 2.28 days) after TKM. During the 29 months of sole TKM treatment period, a CT scan was done four times, on the 20th of January, 2016, the 20th of July, 2016, the 21st of December, 2016, and the 1st of December, 2017. All scans did not show a recurrence of

endometriosis. The serum CA-125 level on the 21st of December 2016 was 33 which was within normal range. **Conclusion:** This case presents the therapeutic potential of TKM for inhibitory effect on the recurrent endometriosis after laparoscopic excision and hormone therapy. This study will be a basis for future clinical research related to endometriosis and can suggest a method for preventing recurrence after conventional therapy.

GYNECOLOGICAL ONCOLOGY

P093

SKENE'S GLAND ADENOCARCINOMA: A RARE FORM OF PRIMARY VAGINAL CANCER

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Problem statement: Primary vaginal adenocarcinoma is a rare entity, comprising only 1% to 2% of all gynecological malignancies. Adenocarcinomas may arise in areas of vaginal adenosis, Wolffian rest elements, periurethral glands, and foci of endometriosis. The paraurethral glands or Skene's glands, are adjacent to the distal urethra. There are few cases reported in literature of Skene's gland adenocarcinoma, typically affects middle-aged and elderly women. The common clinical presentation includes unspecific symptoms such as painless urethral bleeding, enlarged peri-urethral mass and focal tenderness. Due to its rarity and vague presentation, delayed diagnosis may occur. **Methods:** We report a case of an occult neoplasia, with histologic finding of adenocarcinoma in a pelvic ganglionic adenopathy, which reveals as a primary Skene's gland clear cell adenocarcinoma. **Results:** A 52-year-old woman, smoker, with no other significant medical history, presented with dyspnea, fatigue and a major weight loss in the last 6 months. Observation and complementary tests revealed bilateral segmental thromboembolism. Given the clinical picture, the hypothesis of an occult neoplasia was considered. Positive findings were microcytic anemia, relative eosinophilia and increased LDH, β_2 -microglobulin, CA 15-3 and CA125. Pelvic MRI showed "multiple pelvic enlarged lymph nodes, with one node located at the anterior wall of the vagina, with involvement of the urethra. Following this finding, a gynecological examination was requested and showed a left para-urethral mass with 7 cm, solid and painless, at the location of the Skene gland. Urethroscopy did not show any suspicious lesions on the urethra and bladder mucosa. The first vaginal biopsy was inconclusive. The percutaneous biopsy of the right external iliac adenopathy was positive to adenocarcinoma metastasis. A second deeper biopsy of the vaginal mass was performed and confirmed clear cell adenocarcinoma. Due to a stage IV disease, the proposed treatment was palliative chemotherapy. **Conclusion:** Skene's Gland adenocarcinoma is an extremely rare malignant tumor. If metastases are present (such as to the local lymph nodes) then the prognosis is poor.

P094

USE OF SOLUBLE MESOTHELIN-RELATED PEPTIDE AND FOLATE RECEPTOR ALPHA IN EVALUATION OF ADENEXAL TUMORS

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Problem statement: In last two decades, many research projects have been carried out to develop relevant methods to enhance preoperative diagnosis of ovarian cancer. Risk of Ovarian Malignancy Algorithm (ROMA) and IOTA-ADNEX score calculation are well-established in evaluation of adnexal tumors. Nevertheless,

large effort is made to discover new potential biomarkers of ovarian cancer. Among potential markers of particular interest are of Soluble Mesothelin-Related Peptide (SMRP) and Folate Receptor Alpha (FRA). **Method:** Serum samples were preoperatively collected from patients qualified for surgery due to pelvic mass. Among 107 patients recruited to the study (68 pre- and 39 postmenopausal), 33 occurred to suffer from ovarian cancer and 74 had benign ovarian tumors. Serum levels of SMRP and FRA were determined and, subsequently, compared with histological findings of adnexal tumors. **Results:** Concentrations of FRA were significantly higher in sera of women suffering from ovarian cancer compared with patients with benign disease in the groups of all patients ($p=0.0003$) and postmenopausal patients ($p=0.001$). Levels of FRA in sera of patients with serous ovarian cancer were significantly higher than in other histopathological types of ovarian cancer. FRA levels did not show any relevant difference in premenopausal patients with malignant and benign tumors. SMRP concentrations showed no relevant difference between patients with ovarian cancer and benign disease ($p=0.1104$). **Conclusion:** FRA reveals some potential to become a biomarker of ovarian malignancy as its levels in sera of patients with ovarian cancer (especially serous type) are elevated. SMRP did not prove its utility in the diagnosis of ovarian cancer.

P095

COMPARISON OF HISTOLOGICAL OUTCOMES FROM PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN WITH REPORT OF CERVICAL CYTOLOGICAL ABNORMALITY

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Objective: The aim of this study is to compare and investigate the histological outcomes between premenopausal and postmenopausal women with report of cervical cytological abnormality. **Materials and Methods:** From January 2010 to May 2018, patients with abnormal cervical cytology followed by histopathologic examination were collected from Department of Obstetrics and Gynecology of Haeundae Paik Hospital. The patients were divided into two groups according to menopause status and the histologic results of the two groups were compared. This study included the following cervical cytological abnormalities: atypical squamous cells of undetermined significance (ASC-US), cannot exclude high-grade squamous intraepithelial lesion (ASC-H), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL). **Results:** The results of the cervical cytology among the 438 premenopausal women were ASC-US (n=91), LSIL (n=90), HSIL (n=193) and ASC-H (n=64). The results were ASC-US (n=12), LSIL (n=21), HSIL (n=63) and ASC-H (n=19) in 115 postmenopausal women. According to cytology results, we divide into the two group, ASC-US and LSIL were classified as low risk group, ASC-H and HSIL as high risk group. Within the low risk cytology group, HSIL was 73.5% (133/181) by histologic biopsy in the premenopausal group and 42.4% (14/33) in the postmenopausal group. This was 88.7% (228/257) in the premenopausal group and 70.7% (58/82) in the postmenopausal group within high risk cytology group. In both comparisons, there was a statistically significant difference between premenopausal and postmenopausal women. **Conclusion:** In conclusion, our comparative study's findings showed significant difference in correlation of cytology and histology results from premenopausal groups and postmenopausal groups with cervical cytology abnormality. On the basis of this result, we think that since cytological results in postmenopausal women than premenopausal women have low sensitivity, follow up pap smear with high risk HPV testing would be a more conservative management and appropriate than immediate colposcopic biopsy. This may be more significant due to our aging population and as the proportion of older women participating in PAP smear is likely



to increase in future. Keywords: PAP smear, pre-menopause, menopause, High squamous intraepithelial lesion(HSIL)

P096

OUTCOME OF PATIENTS WITH CERVICAL CANCER REFERRED FOR TREATMENT AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL (CMJAH) FROM FAR EAST RAND HOSPITAL (FERH).

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Problem statement: Cervical cancer is a common malignancy worldwide and in South Africa. It remains a burden in developing countries where 80% of cases are diagnosed. Patients with cancer are treated in specialized centers in our setting. The aim of our study was to look at challenges encountered when referring patients from FERH (secondary hospital) to CMJAH (tertiary hospital) and the overall outcomes. **Methods:** This is a retrospective cross sectional descriptive study. We looked at patients with cervical cancer from January 2012 to December 2016. Patients were initially seen at FERH then referred to CMJAH for continuation of care after histology confirmation of the disease. 40 patient's files were retrieved at FERH and only 33 files were found at CMJAH. One year follow up after treatment initiation was done. **Results:** 100% of our patients had cervical squamous cell carcinoma. 6.1% were at stage IB, 33.3% at stage IIB, 9.1% at stage IIIA, 33.3% at stage IIIB, 12.1% at stage IVA, 6.1% at stage IVB. The median time interval from Pap smear to treatment initiation (in days) was as follow: 17(5-138) from Pap smear to cervical biopsy, 42(33-65) from biopsy to biopsy results, 7(0-23) from biopsy results to CMJAH referral, 7(0-22) from CMJAH to date seen at radiation oncology unit, 52(37-79) from radiation oncology to treatment initiation. 6.06% of patients had surgery plus vault radiotherapy, 66.67% had radiotherapy, 21.21% had chemoradiation, 12.1% had palliative treatment. Overall, 6.06% of patients died, 21.21% had palliation care, 3.03% had cancer recurrence, 36.34% had cancer remission, and 33.33% were lost to follow up. **Conclusion:** Our study has demonstrated that the time spent from Pap smear to treatment initiation was longer than the recommended standards. This is due to multiple factors. Many patients presented with late symptoms of the disease at the initial consultation. There is still a need for cervical cancer awareness campaign, education, as well as a need to increase health resources to deal with this disease.

P097

OVARIAN CANCER IMMATURE TERATOMA TYPE IN PREGNANCY: MANAGEMENT AND FETO-MATERNAL OUTCOMES

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Problem Statement: Immature teratoma is malignant ovarian germ cell tumors (MOGCTs). The case in pregnancy is very rare which less than 1% of all ovarian teratoma cases. **Methods:** This study was a case report, which in it we had already done in the clinical setting at Sanglah General Hospital. **Result:** Thirty one y.o. female G2P1A0, 8 weeks 1 day pregnancy, was diagnosed ovarian solid tumor 15x15x15 cm in size. At gestational age (GA) of 19 weeks 5 days, the size of tumor increasing rapidly become 30x30x30 cm. Alfa fetoprotein raise 699.9 IU/mL and LDH 579 U/L. Patient had primary conservative left oophorectomy, omentectomy,

and ascites fluid cytology with histopathological conclusion grade II immature teratoma of left ovary contain immature neuroepithelial and fat component. Magnetic resonance imaging (MRI) at 25 weeks 3 days GA, there was no spreading. Amniocentesis performed at 27 weeks 2 days GA, the fetus had normal 46 chromosome and sex XX without major structural abnormality. Patient had BEP chemotherapy start at 27 weeks 2 days GA. Patient in labor at 40 weeks 2 days GA. Female baby had spontaneous delivery with 2700 grams in body weight without congenital abnormality. Complete surgical staging performed at 58th days postpartum and histopathological result there were no malignant cell anymore, but post-chemotherapy ovarian atrophy feature had found on contralateral ovary. Patient showed psychosocial problem including post-chemotherapy depression and premature ovarian failure (POF). Immunohistochemistry (IHC) ER and PR of teratoma tissue showed immature component had ER (-) and PR (+). Follow up of the baby was in good condition. **Conclusion:** BEP chemotherapy become regimen choice for this case with fetal outcomes was good, but there was POF sign on the mother. Survival of patient on this case is 62%, free recurrence survival post BEP 84% and progressivity post complete surgical staging 8% without delay the chemotherapy. **Keywords:** Pregnancy, BEP chemotherapy, premature ovarian failure (POF), surgical staging, immature teratoma

P098

EFFICACY OF A NON-HORMONAL MUCOADHESIVE VAGINAL GEL IN THE SYMPTOMS OF VAGINAL ATROPHY IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER IN TREATMENT WITH AROMATASE INHIBITORS

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Problem statement: Symptoms of vaginal atrophy are prevalent among women with breast cancer in treatment with aromatase inhibitors due to the estrogen depletion produced in consequence. Vaginal moisturizers are the first-line therapy to relieve these symptoms. This study evaluates the efficacy of a non-hormonal polycarbophilic vaginal gel on severe and bothersome vaginal symptoms in these women. **Methods:** This is a prospective study were 11 postmenopausal women with breast cancer in treatment with aromatase inhibitors and moderate to severe vaginal dryness received 1g of a mucoadhesive moisturizing vaginal gel daily for 3 weeks and twice weekly up to 12 weeks. Presence of symptoms of vaginal atrophy (vaginal dryness, dyspareunia and pruritus) and their intensity were individually scored from 0 (absent) to 3 (severe) at baseline, week 3 and week 12. Total Symptom Score was calculated summing individual symptom scores in every visit. Mean score changes vs baseline were assessed using Wilcoxon test. Safety and tolerability were also evaluated. **Results:** Moisturizing vaginal gel improved the intensity of all vaginal symptoms. Mean changes in vaginal dryness between baseline-week 3 and baseline-week 12 significantly improved from 2.7 to 1.9 ($p=0.031$) and to 1.8 ($p=0.035$), respectively. Total Symptom Score also significantly improved vs baseline from 6.6 to 5.3 at week 3 ($p=0.031$) and 4.4 at week 12 ($p=0.023$). The intensity of dyspareunia and pruritus was also improved. No significant adverse events were shown. **Conclusion:** These results show the efficacy of this mucoadhesive vaginal gel in the significant relief of symptoms of vaginal atrophy in a particularly severe population, showing an early effect after 3 weeks that was maintained up to the end of treatment.

P099

MYXOID LEIOMYOSARCOMA OF THE UTERUS: A CASE REPORT AND REVIEW OF LITERATURE

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Problem Statement: A 32-year-old woman, gravida 1, para 1 was admitted with a 3-month history of abdominal pain and bloating. There were no systemic bladder or bowel symptoms. She has never had a cervical screening test. Her gynaecological history including menstrual cycle was otherwise unremarkable. Abdominal examination revealed a 10x12cm firm non-tender pelvic mass. On vaginal examination, a firm mass was felt occupying the whole pelvis and the uterus was not felt separately. CA 125 was 135U/ml and the remaining tumour markers were within normal range. Computed tomography demonstrated a mass arising from the uterus with multiple nodules. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. **Results:** Histopathology of the specimen showed multiple large tumour nodules ranging from 3 x 3cm to 11.5 x 11cm in size. The cut surfaces of the tumours showed myxoid, gelatinous, pale grey areas. The tumour nodules seemed to invade the uterine myometrium making it difficult to distinguish between normal myometrium and tumour tissue. The mitotic count was two in 50 high power fields. There was no evidence of nuclear pleomorphism or tumour necrosis. The cervix, both tubes and ovaries were normal. The final diagnosis of myxoid leiomyosarcoma was made. Although the tumour showed low mitotic activity it had been categorized as leiomyosarcoma, due to extensive myxoid appearance and infiltrative growth pattern. Postoperative period was uneventful. The patient received external radiotherapy. She has been regularly followed up with no features of recurrence for 2 years. **Conclusion:** Uterine myxoid leiomyosarcoma is a rare mesenchymal tumour with an incidence of 0.3 to 0.67 per 100 000 women, characterized by a gelatinous appearance due to copious amounts of myxomatous stroma. The presence of myxomatous stroma is an indicator of poor prognosis even in the face of low mitotic activity. Even though the commonest presentation is abnormal bleeding, our patient presented with a pelvic mass without any menstrual irregularities. A better prognosis is associated with premenopausal status, circumscribed margins and low mitotic counts and all of these features were present in our patient.



P100

A RARE CASE OF OVARIAN MIXED GERM CELL TUMOUR WITH POLYEMBRYOMA, YOLK SAC TUMOUR AND MATURE TERATOMA

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Background: Polyembryomas are exceedingly rare immature germ cell neoplasms, with recapitulation of embryoid bodies where yolk-sac, embryonal and teratoma components can be found. **Case Report:** A 21-year-old lady presented with abnormal uterine bleeding, increased serum bHCG post unprotected sex, and was initially thought to be an ectopic pregnancy. Imaging showed an adnexal mass and was very suggestive of an Ectopic pregnancy. Laparoscopy revealed normal fallopian tubes and a right ovarian mass. A straightforward right ovarian cystectomy was performed. Histology revealed a 5cm right ovarian cyst with malignant mixed Germ Cell Ovarian Tumour with a predominant Polyembryoma component. Additional testing revealed elevated serum levels of bHCG, AFP and LDH, which were downward trending post-operatively. On discussion with the Gynaecological Oncology team, a further laparoscopic staging with right salpingo-oophorectomy, left ovarian cystectomy and ovary biopsy, right diaphragmatic peritoneum biopsy, omental biopsy and peritoneal washings were performed. Histopathology showed mixed malignant germ cell tumour (90% polyembryoma/yolk sac, 10% mature teratoma), with negative peritoneal washings and negative biopsies of left ovary, diaphragm, and omentum (stage 1C2). The patient was subsequently commenced on adjuvant chemotherapy. **Discussion:** Almost all reported cases of polyembryomas consist of other tumour types, with predominantly yolk sac components in combination with immature or mature teratoma. A literature search has not revealed any cases of polyembryomas with similar composition to this case. And this is also an unusual presentation with unusual imaging findings. Polyembryoma tumour markers include HCG from syncytiotrophoblastic cells and AFP from cuboidal cells of the yolk sac cavity and hepatoid tissue. Treatment of polyembryomas usually involves surgery followed by chemotherapy, though one case reports conservative management with serial tumour markers and imaging studies to avoid aggressive chemotherapy.

P101

RECURRENCE RATES AFTER PELVIC GYNAECOLOGIC NEOPLASMS AND LYMPH NODES AS PREDICTORS

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Problem statement: The authors wanted to know the level of prediction of invaded lymph nodes in the appreciation of recurrence of genital cancers. We performed a study highlighting the loco-regional and lymph node recurrence, after the radical interventions. **Methods:** We searched for the number of invaded lymph nodes from the area in which lymphadenectomy was performed and we also used the technique of the sentinel lymph node. In the First Clinic of General Surgery and Surgical Oncology, a clinic with 70 hospital beds, of the Bucharest Oncology Institute, in Bucharest, Romania, in a 5 year time interval (1/01/2012-31/12/2017), we studied cancer recurrence after the standardized oncological surgical techniques in pelvic gynecologic cancers, performed by general surgeons specialized in surgical oncology. The degree of relapse was associated with the number of invaded lymph nodes at the moment of the first surgical procedure. **Results:** Out of the total of 2100 patients operated on with the radical interventions for



cervical cancer, ovarian cancer and cancer of the uterine corpus during a period of 5 years, the recurrences encountered were around 20%, and we could relate them with the number of invaded lymph nodes. **Conclusions:** The authors consider that the recurrence rate is associated with the number of invaded lymph nodes and with the position of the sentinel lymph node. We believe that the wider use of the technique of sentinel lymph node in pelvic gynecologic surgery could lead to the decrease in unnecessary complications.

P102

THE REPRODUCTIVE OUTCOMES OF 109 SURVIVORS OF MALIGNANT OVARIAN GERM CELL TUMORS

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Problem statement: Malignant ovarian germ cell tumors (MOGCT) usually arise in young women, accounting for 1 to 2% of all ovarian malignancies. Until the 1970s before systemic chemotherapy was established, MOGCT was a disease with a very poor prognosis. However, after the chemotherapy consisting of bleomycin, etoposide, and cisplatin (BEP) was adopted to MOGCT treatment, the prognosis was dramatically improved. Moreover, because BEP therapy has little effect on ovarian function, most patients of MOGCT can preserve their fertility and give birth. However, how many survivors actually got pregnant remains unknown, because there is a vacant period from MOGCT treatment to getting pregnant by the rising age of first marriage and first childbirth. In this study, we aimed to clarify the reproductive outcomes of MOGCT survivors by using data from our multi-center database and their additional survey. **Methods:** From the database between 1986 to 2016, MOGCT patients under 45 years old who received fertility-sparing treatment were picked out, and a questionnaire on reproductive outcome was sent to the registered facilities. In the questionnaire, we obtained the information on marital status, wish for pregnancy, delivery and childbearing, menstrual status, pregnancy complications and birth weight of their children. **Results:** Of the 5,057 patients with any malignant ovarian tumor, there were 115 MOGCT patients with fertility-sparing treatment. The median follow-up period was 10.4 years. After excluding 6 cases of death or loss of fertility by post-recurrent treatment, 109 cases were subject to reproductive outcome analysis. Tumor type was comprised of 41 immature teratomas, 38 undifferentiated germ cell tumors, 27 yolk sac tumors and 3 malignant transformations of mature teratoma. An additional survey revealed that 42 (93.3%) patients had got pregnant among 45 patients who had wished for childbearing. The total number of pregnancies was 65, and a total of 55 babies were born to 40 MOGCT survivors. **Conclusion:** The reproductive outcome of MOGCT survivor is promising.

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RARE PATHOLOGY OF A MALIGNANT UTERINE MYXOID LEIOMYOSARCOMA WITH OSTEOCARTILAGINOUS DIFFERENTIATION

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Problem Statement: Uterine leiomyosarcomas are a rare form of uterine tumours and are often associated with poor survival prognosis. Heterologous differentiation in leiomyosarcomas is an extremely rare phenomenon with less than 15 cases reported in literature to date. We report a case of primary myxoid leiomyosarcoma of the uterus with osteocartilaginous

differentiation. **Methods:** A 44-year old Chinese female first presented to our hospital with complaints of irregular heavy periods and was found to have iron-deficiency anaemia for which she was treated with blood transfusions and iron replacement therapy. She then underwent a dilatation and curettage which revealed a benign endometrial polyp on a background of late proliferative endometrium. A pelvic ultrasound was performed and she was found to have multiple uterine fibroids with the largest one measuring 4.8x4.7x4.5cm. She opted for conservative management but repeated follow up scans showed the fibroid enlarging in size to 8.9x8.5x7.4cm over a period of 2 years. She then underwent a Magnetic Resonance Imaging (MRI) of the pelvis which suggested a large degenerative uterine fibroid. In view of enlarging size of fibroid, she was advised for surgery and underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. **Results:** Final histology showed a malignant neoplasm with areas of myxoid leiomyosarcoma and smaller areas of osteosarcomatous and cartilaginous differentiation, raising the alternative diagnosis of malignant mesenchymoma arising from the uterus. She was discussed at the gynae-oncology tumour board meeting and was planned for full cancer staging versus close observation. The patient opted for close observation. Her post-operative Computed Tomography (CT) scan of the chest, abdomen and pelvis was clear with no evidence of lymphadenopathy or distant metastasis. She is on regular surveillance with symptom review, physical examination and serum CA 125 every 3 months and she has remained disease-free for 12 months so far. **Conclusion:** Osteocartilaginous differentiation of a malignant uterine myxoid leiomyosarcoma is extremely rare and to our knowledge, is the first reported in literature. Due to its rarity, there is insufficient data to suggest the optimal management for cases with such unusual histology.

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PRIMARY CULTURE OF HUMAN ENDOMETRIAL CELLS AS A MODEL TO STUDY TISSUE-RELEASED IMMUNOREGULATORY FACTORS

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Problem statement: Immunomodulatory factors present in microenvironment of endometrium are the important components regulating biological function of the uterus. Indoleamine2,3-dioxygenase enzyme (IDO) contributes to regulation of immune suppression in endometrium by tryptophan depletion and kynurenine generation. RAGE (receptor binding advanced glycation end-products) activation is another mechanism providing immunoregulatory factors such as cytokines. Understanding of the mechanisms leading to endometrial abnormalities might bring us closer to novel cancer therapeutic options for or impaired receptivity of endometrium. This requires proper models suitable for research. Here we present the patient-derived primary endometrial cells cultured as a model for studying immunoregulatory events within endometrial microenvironment. **Methods:** The cells were isolated from cancerous and non-cancerous endometrial tissue during the surgical intervention. The *in vitro* cultured cells were cultured in the optimized medium supplemented with factors promoting growth of epithelial cancer cells. The cell proliferation rate was determined along with morphology. Immunofluorescence was used to test the expression of epithelial marker (CytK8) and MUC1 (abundant in endometrium).

The presence of immune regulatory proteins, like IDO and RAGE were determined by IF and Western Blotting. In addition, kynurenine accumulation in the medium from cultured cells was analyzed by HPLC. **Results:** The human primary endometrial cells isolated from cancerous tissue showed higher propagation capability compared to the control tissue (as expressed by the number of passages carried and amount of the achieved cell number). The size and morphology were quite diverse showing a mixture of epithelial-like and fibroblastic cells. Abundant staining with CytK8 antibodies (often overexpressed on the cancer epithelial cells) was seen in all cultures confirming substantial population of the positive cells in the isolates. MUC1 protein was also seen in cultures independently of disease status. Finally, the immune regulatory proteins, i.e. IDO and RAGE were also detected by IF and WB, although at different level dependent on culture. Importantly, the cells isolated from cancerous tissue released higher amount of KYN into the medium, indicating the enhanced tryptophan metabolism. **Conclusion:** The *in vitro* expanded primary human endometrial cells might be used as a model to study local immunoregulatory proteins IDO and RAGE involved in biology of endometrium

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THE EXPRESSION OF VASUCULAR ENDOTHELIAL GROWTH FACTOR IN SURGICAL SPECIMENS OF PATIENTS WITH RECURRENT/RADIORESISTANT CERVICAL CANCER

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Problem statement: Vascular endothelial growth factor (VEGF) inhibitors have been utilized for treatment against advanced or recurrent cervical carcinoma as a new therapeutic modality. However, the expression level of VEGF in post-radiotherapy relapsed/persistent cervical cancer has yet to be elucidated. The aim of this study was to investigate the expression of VEGF and related molecules using tumor samples from patients with post-radiotherapy relapsed/persistent cervical cancer. **Methods:** From a database of 826 patients who were treated in our institution between 2003 and 2015, we identified eight patients with post-radiotherapy relapsed/persistent cervical cancer, and 20 patients who underwent initial surgery alone as a control. Using samples from these patients, the expressions of VEGF-A, VEGF receptor-1 (VEGFR-1), and hypoxia inducible factor-1 α (HIF-1 α) were immunohistochemically categorized as negative or weakly, moderately, or strongly positive according to the size of the staining area and intensity. **Results:** In carcinoma cells, the expressions of VEGF-A, VEGFR-1, and HIF-1 α were significantly higher in post-radiotherapy relapsed/persistent cervical cancer than control patients (P 0.001, 0.001, and 0.001, respectively). In stroma cells, we observed similar tendencies with significance (P = 0.001 and 0.001, respectively). In addition, the expressions of VEGF-A and VEGFR-1 in carcinoma cells were significantly correlated with each other (P 0.001). **Conclusion:** A significantly higher expression of VEGF was identified in post-radiotherapy relapsed/persistent cervical cancer compared with typical specimens from cervical cancer. The findings provide a new insight into clinical treatment for recurrent/persistent cervical cancer using a VEGF antagonist.

OTHER

P106

EMERGENCY CONTRACEPTION AMONG YOUTH POPULATION

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Problem statement. Every fourth young woman in Russia has had sexual intercourse by the age of 17, around 40% of them did not use any method of contraception. Emergency contraception (EC) among young people in most cases can prevent unplanned pregnancy. **Objective.** To determine of frequency of EC use and awareness of EC among young people. **Methods.** The method of questioning was used (36 items). There were questions about gynecological anamnesis, experience in EC usage (female respondents only) and theoretical knowledge of EC (all participants). The questionnaire was presented in social networks and on paper carriers. The questionnaire was filled by 952 young persons (female – 802 (84.2%), male –150 (15.8%)) from various educational institutions, young doctors of different specialties, others. Mean age was 20.7 \pm 1.6 years (from 15 to 24 years). The group was a simple random sample. **Results.** Almost 10% of young women had pregnancy in the past, half of them were unplanned. Two thirds of unplanned pregnancies ended with medical abortions. One third of female respondents (32.9%) has used EC at least once, in all the cases they preferred levonorgestrel pills. The prevalence of EC usage grew with the increase of the respondents age. The majority of participants think that administration of EC is justifiable if unprotected sexual intercourse has taken place. Up to 65% of respondents know the right regimen of EC administration, a quarter of the participants have incorrect information, others were unable to answer. The greater part of all participants (63%) have incorrectly assume that repeated use of EC leads to infertility and reduction of effectiveness of EC methods. No one was aware of the possibility of an emergency intrauterine contraceptive introduction after unprotected intercourse. Knowledge of EC among schoolchildren and students of non-medical institutions was the lowest. **Conclusions.** Young people in Russia are highly aware of the existence of EC as such, but they have insufficient knowledge of it. It is highly important to give special lectures on family planning and contraception in schools and universities as it helps young people to maintain their reproductive health by using safe and effective methods of contraception.

P107

UTERINE ARTERY PSEUDOANEURYSM EMBOLIZATION: CASE REPORT.

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Problem statement: Uterine artery pseudoaneurysm is a rare cause of late postpartum hemorrhage and is potentially life-threatening, with the prevalence of 2-3 cases/1,000 deliveries. Unlike the actual aneurysm, pseudoaneurysm does not involve the three layers of the blood vessel wall. Typically, it occurs in consequence of a local trauma with vascular injury, usually associated to the use of forceps, caesarean section, and uterine curettage. The forms of this complication can vary from an asymptomatic form to cases of severe haemorrhage. We reported a case of bleeding in late postpartum secondary to uterine artery pseudoaneurysm subjected to arteriography with embolization. **Methods:** A case report of a 35 years old woman with a uterine artery pseudoaneurysm treated with selective embolization through arteriography at Instituto de Medicina Integral Professor



Fernando Figueira (IMIP), Pernambuco, Brazil. **Results:** Patient evolved with critical genital haemorrhage in the third month of postpartum (caesarean section). Initially, the medical staff performed some clinical support procedures and venous infusion of crystalloid. Because of patient's hemodynamic stability, there was no need to perform a hemotransfusion. She was submitted to a transvaginal ultrasonography, which evidenced a right uterine artery pseudoaneurysm. She was then subjected to a selective arteriography of iliac and hypogastric arteries, and embolization of right uterine artery with Histoacryl 33%. There was no clinical complication in patient's postoperative evolution, and she was discharged two days after the procedure, with satisfactory improvement of her clinical state. **Conclusion:** Many factors may cause late postpartum hemorrhage, and uterine artery pseudoaneurysm is an important aspect to be considered, because of its potential consequences. It can be promptly diagnosed through a transvaginal ultrasonography, and can have sensibility and specificity similar to an arteriography. However, arteriography is still the gold standard for diagnosis and treatment. Embolization treatment is an effective option for handling a uterine artery pseudoaneurysm, since it is minimally invasive and does not affect fertility, having a global success rate close to 90%, with a complication percentage around 10%.



P108
INCIDENCE OF EMERGENCY PERIPARTAL HYSTERECTOMY AT A GERMAN TERTIARY PERINATAL CARE UNIT DURING THE LAST 13 YEARS

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Problem: Peripartum hysterectomy (PH) is an emergency procedure for managing life-threatening abnormal uterine bleeding and feared by many obstetricians. We analyzed all performed PHs in a German University Hospital in the last 13 years for presenting actual data on prevalence of PH, reasons for surgery and complications. **Methods:** At the tertiary care center of the Department of Gynecology and Obstetrics at the University Hospital Ulm 41 emergency PH were performed between 2004 and 2016. Recorded data from all patients were retrospectively analyzed regarding patient characteristics, surgical details and outcome. **Results:** The incidence of PH in our hospital was 12.8 per 10.000 deliveries and mostly followed after Cesarean section (80.5 %). The majority of PHs were performed because of abnormal placentation (53.7%; n = 22), uterine atony (26.8%; n = 11), uterine lacerations (14.6%; n = 6) and in rare cases uterine infection (4.9%; n = 2). Clinically relevant intra- and/or

postoperative complications occurred in 53.7% of patients (n = 22) with an overall mortality rate of 2.4 %. Incidence of PH was rising from 0.05 PH per 100 deliveries in 2004 to 0.3 PH per 100 deliveries in 2016 (9 PH in 2016). **Conclusion:** Incidence of PH was considerably increasing during the last ten years at our German university tertiary perinatal care center. With abnormal placentation as leading cause for PH, rising numbers of PH suggest association with the elevated rates of C-sections during the last decade. Through to the high morbidity and mortality of this procedure our findings have significant implications in clinical routine and should generate awareness of obstetricians for this emergency scenario.

P109
ADENOMATOID TUMOR OF THE OVARY: A RARE REPORT
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Problem statement: Adenomatoid tumors (ATs) are rare, benign lesions of mesothelial origin. They occur mainly in reproductive organs, most commonly during the reproductive years. In women, they are more frequent in the myometrium and are the most common benign tumor of the fallopian tubes. AT is uncommon in the ovary and only a very limited number of cases were reported. We will describe a case of ovarian AT, in a postmenopausal woman. **Methods:** Case report. **Results:** A 67-year-old, asymptomatic woman (gravida 2, para 2), was referred to our institution for adnexal mass. She was postmenopausal from age 52 and had a personal history of hypertension. Familial history was not relevant and physical examination was unremarkable. Ultrasonography revealed a 52x33x40mm right ovarian cyst. The mass had a multilocular cystic appearance (8 locules), thin septum and minimal flow (color Doppler 2). The uterus and the left ovary were normal in size and morphology. No free pelvic fluid was noted. The tumor marker CA 125 was in the normal range. The patient kept a regular sonographic and analytic surveillance, until an increase in size was noted, one year later. Subsequently, a laparoscopic right anexectomy was performed. Histological examination showed a multicystic AT of the ovary. No abnormality was identified in the fallopian tube. Up to 6 months after excision no recurrence was detected. **Conclusion:** Ovarian AT is an extremely rare tumor, almost always incidentally diagnosed, without specific symptoms. They have benign behavior and there are no reports of malignant transformation. Surgical excision tends to be curative. Some tumors may mimic malignant tumors, due to the multilocular cystic or solid vascularized appearance, being the histological diagnosis fundamental.

P110
TREATMENT OF VULVAR HAILEY-HAILEY DISEASE WITH LOW-DOSE NALTREXONE

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Problem statement: Familial benign pemphigus, or Hailey-Hailey disease (HHD), is a rare and severe autosomal dominant dermatosis characterized by chronic recurrent vesicles, erosions, and maceration in intertriginous areas. Despite the multiple therapies, such as topical and systemic corticosteroids, systemic immunomodulators, topical and systemic retinoids and laser, HHD can be significantly difficult to control. In non-generalized HHD, there are some case reports of HHD treated successfully with low-

dose naltrexone. **Methods:** We report a case of vulvar Hailey–Hailey disease treated with low-dose naltrexone. **Results:** A 71-year-old white woman presented with multiple large eroded plaques on the vulva (figure 1). She had attempted topical corticosteroids and topical antifungal agents, with no improvement in the symptoms and size of the lesions. She had a 10-year history of painful erosions. She had no clinically family history of HHD. Vulvar biopsy has proven HHD. Treatment with low-dose naltrexone, 3mg nightly, and minocycline was initiated and corticoids were stopped. The lesions began to heal and five months later her skin was with no lesions. There was an improvement in pruritus and pain. She didn't note adverse effects of low-dose naltrexone. **Conclusion:** Low-dose naltrexone may represent an effective and successful treatment modality in HHD without serious adverse effects. Low-dose naltrexone can influence opioid or toll-like receptor signaling and improve calcium mobilization and keratinocyte differentiation. These mechanisms can be responsible for wound healing. More studies are needed to clarify the mechanism and to define the role of low-dose naltrexone for the treatment of HHD. This successful case suggests low-dose naltrexone can be considered a novel therapy for HHD.



P111

A POLICY OF VAGINAL DELIVERY ABOUT MODE OF DELIVERY AMONG HIV- POSITIVE PREGNANT WOMEN IN JAPAN.

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Problem statement: Delivery mode of HIV-positive pregnant women has been strongly recommended elective caesarean delivery since 1984 in Japan. And 55 cases were reported as MTCT-positive through the year of 2016. But since the year of 2000, MTCT-positive cases have been hardly reported on the ground of c-ART and elective caesarean delivery. Then, in other countries, vaginal delivery has been recommended as mode of delivery of HIV-positive pregnant women. **Object:** We, the Group of Epidemiological Study for HIV-positive pregnant women, have been published “New medical guideline for management of HIV-positive pregnant women”. In this new medical guideline, vaginal

delivery is recognized as mode of delivery of HIV-positive pregnant women quite different from traditional recommendation. Then, research has made in acceptance of vaginal delivery of HIV-positive pregnant women in Japan. **Method:** A intention survey was planned about acceptance of vaginal delivery among HIV-positive pregnant women by a questionnaire. **Result:** 418 of 564 HIV-related obstetrics institutions (74.1%) replied to a questionnaire, but 362(64.1%) replies were appropriate for evaluation. The survey showed only 76 institutions (21.0%) could accept vaginal delivery of HIV-positive pregnant women. **Conclusion:** The number of HIV-positive pregnant women is recently 30~40 every year in Japan. And the HIV transmission rate (MTCT) is less than 0.5%. It depends on elective caesarean delivery and preventive management of antiretroviral therapy in early pregnant stage. New medical guideline for management of HIV-positive pregnant women recognized vaginal delivery as delivery mode of HIV-positive pregnant women. But, only 20% of HIV-related obstetrics institutions can accept it. Long and steady research is needed continuously

P112

ATYPICAL MYASTHENIC SYNDROME PRESENTING FOR THE FIRST TIME DURING PREGNANCY – A CASE REPORT

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Problem statement: Myasthenic syndromes can complicate pregnancy but usually respond well to targeted therapy. Sometimes disease progression is atypical entailing challenging pregnancy management. **Methods:** We describe the case of a woman presenting with a myasthenic syndrome during pregnancy. **Results:** We present the case of a 38 year-old primigravida, previously healthy except for a history of asthma and primary infertility of unknown origin, who became pregnant after the fifth course of in vitro fertilization treatments. Of note, she had a positive family history of mitochondrial cytopathy. The first half of pregnancy was unremarkable; however, at 23 weeks of gestation, she developed progressive pathological proximal four-member muscle weakness, dysarthria, dysphonia, dysphagia, and nasal regurgitation of liquids. The patient was admitted to the Neurology Department for further investigation, where she was found to have limb-girdle tetraparesis, nasal speech and bilateral facial paresis without ocular involvement; repetitive nerve stimulation showed an electromyographic decremental response, suggesting a myasthenia gravis diagnosis. She was started on intravenous immunoglobulin while awaiting serologic and genetic test results, but symptomatic improvement was incomplete. Despite additional treatment with pyridostigmine, prednisolone and plasmapheresis, several relapses occurred in the third trimester. Meanwhile, there were no obstetrical complications and fetal growth and development were normal. Increasing refractoriness to therapy, negative myasthenic serology results and a family history of mitochondrial cytopathy put the initial diagnosis into question. In the hopes of halting disease progression, termination of pregnancy was considered and antenatal corticosteroids for fetal lung maturation were administered. Due to progressive and severe neurological impairment, an elective cesarean section was performed at 35 weeks and 4 days of gestational age; a healthy male baby weighing 2570 grams was born. Concurrently, genetic test results led to the diagnosis of DOK7 (docking protein 7) congenital myasthenic syndrome and salbutamol therapy was initiated, with striking clinical improvement over the course of the following months. **Conclusion:** Neurologic disorders first presenting during pregnancy can pose a significant challenge to



neurologists and maternal-fetal medicine specialists alike, requiring close monitoring of disease progression so as to determine the appropriate time and type of delivery.

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ECLAMPSIA, WHEN THE RARE BECOMES COMMON: EXPERIENCE OF A TERTIARY HOSPITAL

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Problem Statement: Eclampsia is a clinical diagnosis based upon the first appearance of generalized tonic-clonic seizures in a pregnant woman with preeclampsia, without a neurologic disease. Occurs in 0,5% of women with preeclampsia without severe features and 1% with severe features. This may arise antepartum, intrapartum and postpartum. The pathogenesis is still not clearly understood. Women at highest risk are nonwhite, nulliparous and on extreme of ages. **Methods:** We conducted a retrospective observational study of the diagnostic of Eclampsia in pregnant women between January 2017 and June 2018. The evaluation was based on personal and obstetric history, risk factors, gestational age at delivery (GA), type of delivery, weight of the newborn and appar rating (AR) at the 5th minute. The data analysis was performed using Microsoft® Excel 2010. **Results:** Seven cases of Eclampsia occurred in unifetal gestation: 4 cases with GA ≤ 32 weeks, 1 case at 35 weeks, 1 case at term and 1 case at postpartum. The incidence was 0,075% (2 cases in 2646 deliveries) in 2017 and 0,37% (5 cases in 1357 deliveries) until June 2018. The average age was 26 years old, most of them in nulliparous and nonwhite women. There was just 1 case with pregnancy-induced hypertension and no history of chronic hypertension. All deliveries occurred by caesarean section (CS) at an average GA of 33 weeks. The newborns average weight was 2024 grams. 2 of the newborns had an AR less than 7 at the 5th minute. **Conclusion:** Our population has an incidence of Eclampsia higher than that described in literature for developed countries, however, there was no maternal-fetal death. Early diagnosis and intervention contributed to the absence of adverse perinatal outcomes. This study warns us about the unpredictability of Eclampsia, that may occur early in pregnancy of young and healthy women. The risk assessment and the early prevention of pre-eclampsia are strategies for reducing the incidence and comorbidities associated to Eclampsia

P114

IS THE "SMUDGED EGG SIGN" DURING THE PERI-OPERATIVE ULTRASOUND SCAN IN ABNORMAL INVASION OF PLACENTA (AIP) ASSOCIATED WITH EXCESSIVE INTRA-OPERATIVE BLEEDING DURING THE TRIPLE P PROCEDURE?

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Problem Statement: Abnormal invasion of placenta (AIP) refers to the invasion of trophoblastic tissue beyond the uterine decidua into the uterine myometrium; uterine serosa or even beyond, involving adjacent pelvic organs. Invasion of trophoblastic tissue through the lower uterine segment into posterior wall of the urinary bladder

obscures the clear 'sonolucent' area between the outline of the bulb of the Foley catheter and the detrusor wall, giving rise to the appearance of a 'Smudged' fried egg during the peri-operative ultrasound scan. This peri-operative ultrasound scan finding is described as the "Smudged-egg sign". The Triple P Procedure is a conservative surgical alternative for AIP and involves a peri-operative ultrasound scan to delineate the upper border of the placenta to facilitate the delivery of the fetus above the upper border of the placenta; pelvic devascularisation and placental non-separation and myometrial excision. The aim of this study was to determine the association between the "Smudged-egg sign" on the peri-operative USS and the amount of intra-operative blood loss during the Triple P Procedure for AIP. **Methods:** A retrospective analysis of 47 cases with AIP who underwent the Triple P Procedure for AIP was performed. Estimated blood loss (EBL) of the group with the "Smudged-egg sign" was compared with the group without this sign during the peri-operative ultrasound scan. Mann-Whitney U Test was used to test the significance of difference in the intra-operative blood loss. **Results:** Out of 47 women, 20 cases had "Smudged-egg sign" on the peri-operative ultrasound scan. Compared to the median blood loss of 1300 ml (IQR=1000-2000) in the control group of 27 cases, the presence of "Smudged-egg sign" was associated with significantly higher median intra-operative blood loss of 2500 ml (IQR = 1850-3225) .U=149.5, p=0.00036 **Conclusion:** Our study suggests that the presence of the "Smudged-egg" sign during the peri-operative ultrasound scan in women with AIP is associated with an excessive intra-operative blood loss. Therefore, we recommend the use of this sign peri-operatively to anticipate excessive intra-operative blood loss in women with AIP.

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EFFICACY AND TOLERABILITY EVALUATION OF A VULVAR GEL INDICATED FOR IMPROVING SEXUAL INTERCOURSES UNDER DERMATOLOGICAL AND GYNECOLOGICAL CONTROL

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Problem statement: The use of stimulating gels for the intimate area in sexual relations is increasing to help make intercourse comfortable, pleasant and recover sensations that even allow prolonging the sexual act. The study objective was to evaluate the efficacy and tolerability of *Libicare® Gel Íntimo*, a non-hormonal intimate vulvar gel for enhancing the sexual experience which is based on natural ingredients: L-arginine, Ginkgo biloba leaf extract, Brazilian ginseng root extract with Arginine L-PCA, hyaluronic acid niosomes and a stimulating complex composed by Panax Ginseng root extract, B6 vitamin, Damiana (*Turnera diffusa*) extract and peppermint oil. **Methods:** Healthy female volunteers aged 18-65 years having 2-3 intercourse per week were included. After signing an informed consent, they applied the tested product on the external genital zone before the intercourse for 28 days. The product could be used with or without condom. Subjective efficacy (favors intercourse, accelerates climax, improves sensory effects, relieves dryness, respectful with skin, easily removed and suitable for use it with condom) was evaluated using a Likert scale of five points, being 1: *strongly disagree* to 5: *strongly agree*, and considering the opinions between 4 and 5 as satisfied. A visual evaluation of the skin of the experimental area and adverse event evaluation were performed by both dermatologist and gynecologist after 4 weeks of application. **Results:** A total of 21 volunteers (mean age 33.95 years) were evaluated. 95% agreed or strongly agreed that the product favors intercourse, relieves dryness and was easily removed. Besides that, 90% indicated the product improves sensory effects, 81% believed that the product was suitable for use it with condom and 67% indicated that the product



use accelerates the climax. According to the clinical examination carried out by the dermatologist and the gynecologist, none of the volunteers presented any alterations related with product use and none of the volunteers indicated undesirable symptoms during product use. **Conclusions:** Libicare® Gel Íntimo shows very good subjective efficacy and excellent tolerability which met expectations of a good intimate gel for 100% the volunteers. Dr Palacios and Dr Losa have been speakers for Procare Health in several meetings.

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EVALUATION OF THE LEVEL OF SATISFACTION FROM PATIENTS USING VAGINAL MOISTURIZERS (IDRAVAG SURVEY)

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Problem statement: Vaginal dryness implies a very frequent use of vaginal moisturizers (VM). This frequency of use requires a vaginal moisturizer to be comfortable to apply while producing satisfactory sensations in women, which directly affects adherence and, ultimately, the effectiveness of the product. The objective of the survey was to know the opinion of health professionals (HP) about the general level of satisfaction from women with the use of the usual VM and about if there is room for new and better designed moisturizers. **Methods:** The Idravag survey was carried out between January and March 2018. A questionnaire of 8 questions related to the use of VM in the usual clinical practice was elaborated. The survey was addressed to HP, gynecologists and midwives, who visit women who use VM, following a homogenous distribution throughout the national territory. A double data entry was made in an Excel file to ensure the quality of them. **Results:** A total of 150 HP participated, 67% of which point that women aging between 50 and 60 are the main users of VM. 86% of surveyed indicate that global satisfaction from patients with the use of these products is good or excellent. The "short duration of the effect", "do not hydrate enough" or "do not contain hyaluronic acid" are the deficiencies most frequently remarked of VM (30%, 23% y 19%, respectively) by HP. The VM are mostly recommended to improve vaginal dryness (43%) and intercourse (41%). 67% of HP allude at least 1 patient with some type of undesirable effect or complaint motivated by a VM, being irritation the most frequent. A moisturizer with hyaluronic acid, prebiotic and aloe vera (Idracare®) would be regularly and always used by 83% and 15% of HP, respectively. **Conclusion:** VM are mainly used after age 50 to improve vaginal dryness or sexual intercourse. Although the satisfaction of patients with VM is good or excellent, these present deficiencies and are not exempt from adverse effects, with irritation being the most frequent one. Most of HP consider there is room for new products specifically designed to obtain the best hydration.

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KNOWLEDGE AND PATTERN OF USE OF EMERGENCY ORAL CONTRACEPTION AMONG PORTUGUESE WOMEN

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Problem statement: Emergency contraception (EC) is used in Portugal for more than 30 years and should be a point of discussion in sexual and reproductive health counselling and also between sexual partners as last resort of undesired/unplanned pregnancy prevention. Objectives: Measure EC use rate; evaluate level of knowledge, information source and attitudes and experience of women related to EC; investigate association between demographic variables and level of knowledge with the intention or priors of use of EC. **Methods:** Transversal and analytical study. Through an original anonymous questionnaire a sample of 132 portuguese women in fertile age (average age 31,9±8,85 years) and with active sexual life were studied. They were users of primary and secondary healthcare. 2 groups were considered: one with previous use of EC or intention to; other without intention to use or undecided. **Results:** 28% used EC, of which 43,2% without any counselling. Despite 95,5% of women claim to have knowledge about EC, from those only 15,2% answered correctly to almost all of the questions (10) about knowledge evaluation (total of 14). The media were the most frequent source of information (58,7%). Most (67,5%) considers that EC is associated to severe adverse reactions; is harmful to fertility (64,3%); is necessary to wait until the next menstrual cycle to initiate a regular contraception method (70,4%); and most also doesn't know the period of time to use EC after an unprotected sexual relation (74,6%). Factors associated to previous use/intention to use EC were being single (p=0,029), priors of voluntary termination of pregnancy (p=0,007) and a greater knowledge about EC (p0,001). **Conclusion:** The low knowledge about EC, especially regarding the correct period of use, place of acquisition and safety were associated to a lesser use, or intention to, of EC in case of unprotected sexual relations. Because of that we consider that health professionals must improve and develop measures to transmit correct information about contraceptive methods, access to family planning care and about EC and it's indication.

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NEW TECHNIQUES TO DEAL WITH COMPLEX SITUATIONS IN OBSTETRICS AND GYNAECOLOGY

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Introduction: Critically ill patients have an increased risk of adverse outcome despite the intensive use of resources. Surgery and supportive care have often been the pillars of management. But surgery has its morbidity and, in some situations may lead to suboptimal outcomes eg a patient with coagulopathy. Interventional radiology, advances in Anaesthesiology, blood banking and imaging are relatively new and innovative techniques helping improve patient outcomes in critical situations Objective To discuss 3 complex scenarios managed in a tertiary care setting in Australia. To discuss the roles played by different disciplines in such situations. To impress on a team approach and the crucial role played by efficient communication and utilization of resources. **Methods:** We discuss 3 case scenarios - Placenta Percreta in a post-caesarean pregnancy invading the bladder mucosa. Postnatal patient with a 2.5-litre retroperitoneal hematoma following vaginal delivery Post Hysterectomy patient with recurrent PV bleeds and an AV malformation. In the first patient, Interventional radiology was combined with Multidisciplinary surgical teams to minimize intra-operative blood loss and make surgery safer and easier for the surgical team. In the second patient, the use of Interventional radiology negated the need for laparotomy, reduced the morbidity of treatment and hastened recovery of the patient. In the third patient, the use of interventional radiology bypassed the need for



operative management for post-op bleed. This, along with surgical & non-surgical methods like ROTEM, their role in difficult situations & their life-saving potential are discussed. A multidisciplinary combined team (MDT) approach helped improve patient safety and outcomes in these situations. **Discussion and Conclusions:** Newer surgical techniques & prompt recognition, planning & coordination can lead to improved outcomes. Use of Interventional Radiology has led to lower blood loss, lesser morbidity, & improved safety in these situations. The role Anaesthesia, Intensive care, Haematology, and associated specialties are crucial in managing these patients. Finally, a multidisciplinary team approach with good planning, communication, and standardized protocols and care bundles are crucial in ensuring optimal outcomes. Lessons learned, recommendations from our experience, and our journey to developing a center of excellence in managing these difficult scenarios are discussed.

P119

INHERITED THROMBOPHILIA IN PREGNANT PATIENTS: A RETROSPECTIVE CLINICAL STUDY

Diana Ioana Voicu
Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest (ROMANIA), Bucharest, Romania

Problem statement: Thrombophilia refers to an abnormality of blood coagulation that increases the risk of thrombosis. Abnormalities of any component of Virchow's triad (circulatory stasis, vascular wall injury or hypercoagulable state) can lead to thrombosis. Most heritable thrombophilias are heterozygous defects. Hereditary thrombophilia arise as a result of over-activity of coagulation factors. The aim of this study was to perform a screening of pregnant women hospitalized in our hospital for hereditary thrombophilia. **Material and methods:** Our study group included 819 pregnant women. Genetic tests for specific mutations included methylenetetrahydrofolate reductase (MTHFR) gene mutation, factor V Leiden mutation, prothrombin 20210 and factor XIII mutation. **Results:** The incidence of high-risk inherited thrombophilias is low in our study, so the frequency of homozygous factor V Leiden mutation (n=2) is equal with the incidence of homozygous prothrombin G20210A (n=2) mutation- 0.24%. The incidence of heterozygous factor V Leiden was 17,09 % (n=140) , heterozygous prothrombin G20210A mutation was 3.29% (n=27) , homozygosity for the C677T polymorphism of methylene tetrahydrofolate reductase mutations was 5% (n=41) , homozygosity for the A1298C polymorphism is present in 3.17% (n=26) of pregnant women included in our study. Also heterozygous methylene tetrahydrofolate reductase mutations (C677T, A1298C) were present at 48.35%. **Conclusions:** Hereditary thrombophilia is a genetic condition of heterogeneous etiology, determined by genetic mutations that have been found in all factors of coagulation. There is no curative treatment for genetic thrombophilia. Pregnant women that presented risk factors for thrombosis and were diagnosed with high risk hereditary thrombophilia received prophylactic anticoagulant treatment. This presentation was supported by the FDI grant no. 0547/2018, funded by National Council for Higher Education, Ministry National Education`

P120

ON UNDERSTANDING THE WOMEN'S DESIRE FOR UTERUS TRANSPLANTATION. A REVIEW

Polychronis Voultsos
Aristotle University of Thessaloniki (Faculty of Medicine), Assistant Professor of Medical Ethics, Thessaloniki, Greece

Problem statement: Uterus transplantation is a breakthrough in the field of assisted reproduction. The goal of this method is pregnancy-related. The desire for uterus transplantation is

necessary for fully addressing ethical issues raised by the implementation of such a risky treatment. We provide some nuanced insight into this desire to better understand it. **Methods:** A systematic review, including the grey literature. **Results:** The desire for uterus transplantation may be based on woman's strong desire to give birth to her own offspring, or to experience the process of gestating offspring to develop, or even just to experience what it feel like for a woman to live a pregnancy. Rigorous scrutiny of recipient's psychology is necessary. Great emphasis should be placed on investigating whether a given applicant has an'intense desire to get pregnant`. It is difficult to assess whether a desire for uterus transplantation is authentic and as such if can justify the risks and the eventual public funding of the method. **Conclusion:** In any given case of prospective uterus transplantation, the second-order desire of a woman who wants to undergo the treatment should be investigated by a multi-disciplinal expert committee.

P121

RETROSPECTIVE STUDY THYROID DYSFUNCTION IN PREGNANCY AND ITS IMPACT ON OBSTETRIC AND NEONATAL OUTCOME IN SUNGAI BULOH HOSPITAL, MALAYSIA

Juliana Yusof
Obstetric and Gynaecology, Faculty of Medicine, University Institute Technology of MARA, Masters of Obstetric and Gynaecology, Sg Buloh, Malaysia

Problem Statement: We aim to determine number of patients with thyroid dysfunction in pregnancy and their obstetric and neonatal outcome **Methodology:** A retrospective study was conducted in Sungai Buloh Hospital from the data obtained by the hospital registry from July 2013 to July 2016 and information regarding the patient's socio-demographic data, anthropometry of the neonate, the variation of the neonatal birth weight and maternal thyroid disorder was recorded in a designed data collection form with the sample size of 166 pregnant mothers. The inclusion criteria for this study were patient's age from 20-40 years old and they do not have chronic diseases such as hypertension, heart disease and diabetes mellitus. Meanwhile neonates selected were those born at 37 weeks to 42 weeks. The exclusion criteria were patient's age less than 20 or more than 40 years old. Neonates born preterm or with chromosomal congenital anomalies were excluded. The collected data was analyzed using (SPSS) version 21. Independent t-test was used to analyze two variables in which one is categorical and the other is numerical. Chi-square was used to analyze two independent categorical variables. Statistical analysis of p 0.05 was use as a significant value. **Results:** 1. There was no significant association of thyroid dysfunction in pregnancy with obstetric outcome such as anemia, Gestational Hypertension, Gestational Diabetes Mellitus, preeclampsia, preterm labour and antipartum haemorrhage. 2. There was no significant association of thyroid dysfunction with neonatal birth weight. **Conclusion:** Thyroid dysfunction in pregnancy did not significantly affect obstetric outcome and neonatal birth weight.

P122

OBSTETRIC CERCLAGE PESSARY: IS THIS AN ELEGANT SOLUTION TO A DIFFICULT PROBLEM?

Shostak D.P., Shostak I.A., Pashov A.I.
State autonomous institution of Kaliningrad «Regional Perinatal Center»; Immanuel Kant Baltic Federal University.

Premature birth currently accounts for 5-10% of the total number of deliveries. Unfortunately, this indicator has no tendency to decline, despite the rather high level of obstetric-gynecological care. One of the causes of premature birth is ischemic-cervical insufficiency, for correction of which at present the obstetric cerclage pessary is



successfully used. The purpose of the study was to identify the appropriateness of using obstetric cerclage pessary as a prophylaxis of premature birth, as well as the problem of overdiagnosis of ischemic-cervical insufficiency (ICI). A retrospective analysis of 100 birth histories for 2017 in the State Autonomous Institution of the Kaliningrad Region Perinatal Center in Kaliningrad was conducted. All women were on the retention of pregnancy in this institution at different terms of gestation, they had an obstetric cerclage pessary. According to the results of the study, preterm labors in the study group were 20%, which exceeds the world statistics. According to direct indications (anatomical ischemic-cervical insufficiency with confirmed ultrasound and anamnestic data), the pessary was established only in 16% of cases, and in 29% of cases - the first-pregnant women! Up to 24 weeks of gestation, obstetric cerclage pessaries were identified by 31 women, most of whom (84%) were delivered on term. 19% of women (mainly, first-born) received cervical ruptures in childbirth. Thus, the obstetric cerclage pessary Dr.Arabin is a modern, convenient and sufficiently reliable method of correction of ischemic-cervical insufficiency, but it should be used only with anatomic ICI on terms up to 23-26 weeks of gestation. Setting it to be first-rate with signs of shortening of the cervix, routine use as a prophylaxis for premature birth, setting for gestation beyond 26 weeks of gestation is not appropriate and, moreover, contributes to the development of infectious complications, cervical ruptures in childbirth and does not reduce the frequency of preterm labor.

P123

PREVALENCE OF POLYMORPHISM OF GENES ASSOCIATED WITH THROMBOPHILIA IN THE KALININGRAD REGION

Shostak D.P., Pashov A.I, Sturov V.G.

*State autonomous institution of Kaliningrad «Regional Perinatal Center»; Kaliningrad, Russia;
Immanuel Kant Baltic Federal University; Kaliningrad, Russia;
Novosibirsk State University; Novosibirsk, Russia*

Thrombophilic conditions are one of the most common causes of obstetric pathologies, such as the syndrome of habitual fetal loss, intrauterine growth retardation, placental insufficiency. A separate group of thrombophilia is caused by hereditary conditions associated with gene mutations. The aim of the study was to analyze the results of testing the gene polymorphism associated with thrombophilia in women in the Kaliningrad region in 2015-2016. With the purpose of optimization and personification of prophylaxis of thromboembolic complications. We examined 70 women planning pregnancy, as well as patients before the appointment of hormonal contraception and menopausal hormonal therapy. Blood coagulation genes, fibrinolysis system genes, folate metabolism genes, and platelet-derived glycoprotein genes have been tested. Clinical methods - PCR mass spectrometry. The most common hereditary thrombophilia are caused by the polymorphism of the plasminogen activator (PAI-1) inhibitor and the tissue plasminogen activator-PLAT, as well as a decrease in folate metabolism. So, according to our data, PAI 1 in 4 times increases the risk of complications of pregnancy. Polymorphism of the prothrombin gene in the heterozygous state is rare (1.9%), but the combination with the Leyden mutation is unfavorable and is a contraindication for the appointment of combined oral contraception, since the risk of thrombosis increases 80 times. The decrease in the activity of folate metabolism enzymes in the study groups was 32%. Thus, a genetic examination is shown to all women who have a history of perinatal loss, a syndrome of habitual fetal loss, thrombotic and thromboembolic complications in themselves or close relatives, and before prescribing combined oral contraception (COC) or menopausal hormone therapy (MGT) for women.





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¹ In a recent clinical study conducted at North Florida OBYGN, Jacksonville, FL, USA & The Springs Medical Center, Louisville, KY, USA, 2017-2016.

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Laser Course

FRIDAY, NOVEMBER 23, 2018



VAGINAL ERBIUM LASER FOR WOMEN'S HEALTH

15:30-18:30		WHITTLE
CAPSULE	Course participants will learn the basic principles of using lasers in a variety of non-surgical procedures within the fields of minimally invasive gynecology. The entire course is constituted of six topics covering the use of FotonaSmooth Erbium laser systems in indications of: Vaginal Relaxation Syndrome (VRS), Genitourinary Syndrome of Menopause (GSM), Stress Urinary Incontinence (SUI), Pelvic Organ Prolapses (POP), Lichen Sclerosus and post Episiotomies scars. Each lecture will last 30 minutes and will have 10 minutes for discussion. Upon completing the End-of-Course Test the participants will receive the Course Certificate	
15:30-15:35	Introduction by program coordinator Zdenko Vizintin, Slovenia	
15:35-16:15	Physical concepts of the application of the lasers in Gynecology and the treatment of Vaginal Relaxation Syndrome Zdenko Vizintin, Slovenia	
16:15-16:55	Laser use in Genitourinary Syndrome of Menopause Marco Gambacciani, Italy	
16:55-17:35	Laser treatment of Lichen Sclerosus et Atrophicus and Pelvic Organ Prolapses (POP) Urska Bizjak-Ogrinc, Slovenia	
17:35-18:15	Laser use in Stress Urinary Incontinence and Episiotomies Aleksandra Novakov-Mikic, Serbia	
18:15-18:30	End-of-Course Test	



Industry Symposium

SATURDAY, NOVEMBER 24, 2018

INFERTILITY/ART/IVF



GEDEON RICHTER

FIBROIDS AND IVF: CAN WE REACH A CONSENSUS?

12:10-13:40		FLEMING
Capsule	The current delay in family planning increases the chances of encountering fibroids and age-related infertility. Which conservative solutions do we have? Despite over 250 studies, the Cochrane summary failed to demonstrate that myomas, which were suspected to affect implantation and pregnancy, were reversed by myomectomy. More studies are needed, but do we have a medical solution?	
Chairpersons	Yacoub Khalaf , <i>UK</i> Jacques Donnez , <i>Belgium</i>	
12:10-12:35	The impact of uterine fibroids on fertility Nikolaos Polyzos , <i>Spain</i>	
12:35-13:00	Treating uterine fibroids in infertile patients Nicole Sanger , <i>Germany</i>	
13:00-13:25	Medical management of moderate to severe uterine fibroids in infertile women Antonio La Marca , <i>Italy</i>	
13:25-13:40	Q&A	



Industry Symposium

SATURDAY, NOVEMBER 24, 2018

GYNECOLOGY



DESCRIPTION OF THE ROLE OF INTRACRINOLOGY FOR THE PHYSIOLOGICAL TREATMENT OF VULVOVAGINAL ATROPHY (VVA)

12:10-13:40		ST. JAMES
Capsule	After menopause, dehydroepiandrosterone (DHEA) becomes the exclusive source of both estrogens and androgens. The decrease in serum DHEA causes a deprivation of intracellular sex steroids which is the main cause of the symptoms of menopause, including VVA. The intravaginal administration of DHEA, by a strictly local action, corrects the symptoms and signs of VVA while all serum steroids remain within normal values, thus avoiding abnormal systemic exposure.	
Chairpersons	Fernand Labrie , <i>Canada</i> Santiago Palacios , <i>Spain</i>	
	Intracrinology – The lack of DHEA, the exclusive source of sex steroids, becomes the main cause of menopausal symptoms, including VVA, in postmenopausal women Fernand Labrie , <i>Canada</i>	
	Healthy and sex steroid-deprived vagina – From preclinical to clinical characteristics Céline Bouchard , <i>Canada</i>	
	Intravaginal prasterone, novel and non-estrogen efficacious therapy for vulvovaginal atrophy Santiago Palacios , <i>Spain</i>	



SUNDAY, NOVEMBER 25, 2018

GYNECOLOGY

14:30-15:00	INDUSTRY SUPPORTED LECTURE	ST. JAMES
14:30-15:00	Countercurrent lecture: Role of local DHEA Phillippe Bouchard , <i>France</i>	



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Atila BioSystems, located at Silicon Valley, California, has developed one of the world best **high-risk HPV detection** products for cervical cancer screen based on novel isothermal amplification technologies (called Ampfire: detects all 15 high risk HPV in single tube format and genotypes HPV 16 and HPV 18 simultaneously). The product is much faster (1 hour from sample to answer) and very simple (no DNA extraction needed) having both CFDA and CE certification. In addition, our extremely high multiplex digital PCR is capable of detection all aneuploidy (NIPT, T21, T18 and T13 in single droplet) from maternal blood and cancer mutation detection (detection of 63 EGFR mutations in single droplet reactions) in liquid biopsy. NIPT using digital PCR is extremely fast and simple without needing sample preparation.



BARCELONA IVF

www.barcelonaivf.com

Barcelona IVF is a Fertility Clinic which focuses on offering a quality personalised service to each of their patients. Their state-of-the-art laboratory and specialized team allows them to have outstanding pregnancy rates despite carrying out elective single embryo transfers at blastocyst stage in the majority of their treatments. Communication is key, and for this reason their patients are assigned one patient assistant and one doctor who will follow them throughout the procedure. And they can keep it simple by coming only once to Barcelona as visits can be programmed via Skype



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www.besinshealthcare.co.uk

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CooperSurgical Fertility Companies: www.origio.com

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The **CooperSurgical** family of fertility and genomics products is comprised of leading brands in IVF and reproductive genetics - ORIGIO, SAGE, LifeGlobal, Wallace, TPC, Humagen, RI, K-Systems and CooperGenomics, providing innovative solutions for the entire ART journey. Working together, we offer a trusted system of consumables and equipment as well as a full suite of reproductive tests and services.

By collaborating with experts in the field, we aim to drive scientific excellence and evolve innovation in line with customer needs by offering tailored product solutions, hands-on training and expert-led workshops.



**ELITE IVF**

www.elite-ivf.com

ELITE IVF is the premium egg donation & surrogacy agency for IVF physicians and clinics around the world. Working with our global network of acclaimed physicians and pioneering researchers ELITE IVF has helped thousands of patients struggling with infertility. Referring to ELITE IVF means peace of mind for you and your patients and increased revenue for your practice. We manage the entire egg donation, semen donation and surrogacy process to perfection – from medical, legal and financial, to travel, shipping and logistics. We believe that being committed to defined standards of excellence and best practices results in the high clinical success rates that our patients deserve.

**ENDOCEUTICS**

www.endoceutics.com

Endoceutics is a private pharmaceutical company operating in the field of women's health and hormone-sensitive cancer prevention and treatment. The firm is the world leader in the field of menopause and sex steroids. Following its approval by the US Food and Drug Administration (FDA) for the treatment of the most bothersome symptom of vulvovaginal atrophy due to menopause, namely dyspareunia and by the European Medicines Agency (EMA) for the treatment of the symptoms and signs of vulvovaginal atrophy, Endoceutics focuses on developing non estrogen-based therapies for the treatment of sexual dysfunction and the other symptoms of menopause, including hot flashes.

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www.medical.escoglobal.com

Esco Medical is the IVF business unit of Esco Group, a global life science tools provider. Esco Medical delivers innovative solutions for fertility clinics and laboratories.

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Most of our products are designed in Denmark and manufactured in the EU. The primary focus of this division is to increase pregnancy success rates and patient satisfaction.





FERRING PHARMACEUTICALS

www.ferring.com

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GEDEON RICHTER

www.richter.hu

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Merck

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Merck is a leader in fertility treatment. Since the 1950's, Merck have provided healthcare professionals and patients with innovative fertility treatment options, devices and advanced laboratory technologies. With a portfolio of fertility drugs and technologies, Merck is a holistic, integrated and innovative fertility provider with the aspiration to support people to fulfil their dream of parenthood. Merck's vision is to develop market innovative products and services which can help infertile couples at every stage of their reproductive cycle: from follicular development to early pregnancy.




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Pantarhei Bioscience (PRB) and **Pantarhei Oncology (PRO)** focus on innovative drug development in Woman's Health (WH) and Endocrine Cancers. PRB has developed a product pipeline based on its ability to identify, confirm and patent protect novel targets and medical uses of existing drugs, hormones, other endogenous human biologicals and combinations thereof. Pantarhei adheres to the highest scientific standards for preclinical and clinical drug development. The current pipeline of Pantarhei includes (i) Androgen Restored Contraception (ARC), adding dehydroepiandrosterone (DHEA) to oral contraceptives, (ii) the fetal estrogen Estetrol (E4) for the (co)-treatment of breast and prostate cancer and (iii) the use of the Zona Pellucida 3 (ZP3) antigen and biomarker for immunotherapy of ZP3 expressing tumors such as ovarian and prostate cancer.


PREIS SCHOOL
www.preischool.com

The PREIS School – (The Permanent International and European School in Perinatal Neonatal and Reproductive Medicine) founded in 2012, is inspired by the values of scientific culture, ethics and bioethics of life sciences and pursues the aim of promotion and enhancement of the fundamental ideals of maternal infant medicine in its entire course: preconceptional, reproductive, maternal and child health periods. Moreover, it asserts and promotes, in every seat, the global culture of health of the mother, the fetus and the neonate, understood as being the achievement of the highest level of mental, physical and social wellbeing.

The School has a permanent home in the prestigious medieval building of the "Istituto degli Innocenti" in Florence, Italy, which was the first Children's Hospital built in Europe, by the master architect Brunelleschi in the 15 century.

The founder and director of the School is Prof. Gian Carlo Di Renzo and the Chairman of the Board Prof. Gianpaolo Donzelli. Members of the Scientific Committee are: Eduardo Fonseca, Renè Frydman, Dominique Haumont, Moshe Hod, Kypros Nicolaides, Michael Robson, Roberto Romero, Umberto Simeoni, Johan Smitz, Christian P. Speer, Yves Ville, Gerard H.A. Visser


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www.cryotech-japan.jp

REPROLIFE provides Cryotech products, the latest technology of vitrification of human oocytes and embryos, created by Dr. Masashige Kuwayama in 2012.

He developed the Cryotec Method by overcoming the 18 weaknesses of his previous work, the Cryotop Method, to achieve a 100% survival rate of oocytes and embryos.

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www.syneron-candela.com

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www.theramex.com

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THE WORLD EGG BANK

www.theworldeggbank.com

The World Egg Bank is the only egg bank worldwide built solely for egg donation. Our unique centralized business model ensures we conduct all egg vitrification with optimized protocols and the same experienced laboratory systems and staff. Our only operational focus is providing quality donor eggs from our custom built, state of the art facility, designed solely for egg freezing. We manage all recruiting, screening, stimulation, retrievals, vitrification, and shipping from our egg banking facility. Most of our donors are open identity with thousands of ova vitrified and ready to ship, and hundreds more young women waiting to donate.



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