



# Center For Advanced Fetal Care Newsletter

Volume 8 Issue 3  
Summer of 2017  
Tripoli - Lebanon

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## Fiamma Inestinguibile - Inextinguishable Flame

...Pains us. Propels us. **Possesses** us. It is precisely that **scorching flame** that pushes us to unreachable boundaries and allows us to break barriers in order to achieve the unfathomable in the pursuit of our **elective affinities**... This has been the case as we relentlessly explore the **galaxies**, as we **reach out to the sun** and as we think of **innovative methods** to utilize the **elements**. Our incessant pursuit of knowledge has now driven us to examine the earliest possible point in time where it may be possible for our species' brain to learn: the **in-utero days!** We thus dedicate this issue to the "inextinguishable flame", that which has allowed us, after decades of tireless research, to finally arrive at a means of screening, and possibly preventing early preeclampsia as evidenced by the ASPRE study, just published in NEJM. We present to you evidence in support of the importance of being ever so vigilant as we introduce new screening modalities as evidenced by the new ISUOG Consensus Statement on cfDNA and Ma et al's letter to the UOG Editor. We review for you the 16th World Congress of the Fetal Medicine Foundation, and the Fetal Care Symposium held at King Faisal Specialist Hospital and Research Center where the latest advances in fetal medicine, internationally and regionally, were presented. We highlight upcoming invaluable learning opportunities from the AIUM, FHS, ISUOG and LSOG in order to fuel the fire and keep the flame alive. We proudly share with you our latest educational endeavor in Lebanon, geared at our residents, in cooperation with ISUOG, in order to ensure the highest possible standards in women's imaging. We sincerely hope that this issue serves as a reminder of what Andrea Gibson once said: "the most fertile lands were built by the fires of **volcanoes**"...



Jean Boghossian



Our Scorching Sun

## Aspirin vs Placebo in Pregnancies at Risk for Preterm PE

The results of the long-awaited ASPRE study by Rolnik et al have been published in the **NEJM**. This multi-center, double-blinded, placebo-controlled study randomized 1776 women at 11-14 weeks, with singleton gestations, at risk for preterm preeclampsia, to either placebo or 150 mg of daily aspirin (not 81 mg!) until 36 weeks. Patients were identified as being high risk based on an algorithm utilizing maternal risk factors, maternal mean arterial blood pressure, PI of the uterine artery, PAPP-A, serum-pregnancy associated protein A and PGF at 11-14 weeks. The study's primary outcome was delivery with preeclampsia prior to 37 weeks and it was analyzed with the "intention to treat" principle. After exclusions due to withdrawal of consent in 152 patients and no known outcome in 4 patients, 1662 women completed the study: 798 in the aspirin group and 822 in the placebo group. There was no statistically significant difference in adverse events affecting neither the neonates nor the mothers in the 2 groups. However, there was a statistically significant difference in the rate of preterm preeclampsia between the two groups: it occurred in 1.6% of those in the aspirin group versus in 4.3% in the placebo group (P=0.004). The time has come to expand screening at 11-14 weeks to identify the high risk patients and commence 150 mg aspirin.



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## LMWH's Effect on Cell Fraction and False Negative cfDNA

As with any mode of testing, false positive as well as false negative results are of the greatest concern. Along those lines comes a most interesting letter to the editor from Ma et al just released as an ePub ahead-of-print in **UOG** in which the authors address the impact of the administration of low molecular weight heparin (LMWH) on fetal cell fraction (FF) in the maternal blood and subsequently, the false negative results of cfDNA. In their letter, the authors report on the drastic changes in the FF in 2 samples of blood taken from the same patient prior to and after the cessation of LMWH. The fetus was confirmed to have trisomy 21 and the cfDNA testing results showed low risk for trisomy 21 with a FF of 1.60% at 19w1d while on LMWH, and a high risk for trisomy 21 with a FF of 5.77% at 21w0d after stopping LMWH. The authors attribute this to LMWH's effect on the placental trophoblasts where it reduces trophoblastic apoptosis and enhances trophoblastic survival altering fetal DNA fraction. This is independent of its anticoagulant effects. As such, the authors advise that great caution should be exercised in the interpretation of cfDNA testing results in high risk pregnancies where the mothers may be receiving anticoagulants.



## Highlights from the “Fetal Medicine Foundations’ 16th World Congress” Held June 25 - 29, 2017 in Ljubljana, Slovenia. By Slama Jabak, MD

The **16<sup>th</sup> World Congress in Fetal Medicine** took place June 25-29, 2017 in Ljubljana, Slovenia. This year’s congress was spectacular by all means. Fetal medicine specialists from all over the world came together to discuss the newest research in fetal medicine. Among the distinguished speakers were Ranjit Akolekar (UK), Ahmet Baschat (USA), Peter Benn (USA), Katia Bilardo (Netherlands), Rabih Chaoui (Germany), Jan Deprest (Belgium), Jon Hyett (Australia), Jacques Jani (Belgium), Anthony Johnson (USA), Oliver Kagan (Germany), Asma Khalil (UK), Liesbeth Lewi (Belgium), Liona Poo (Hong Kong), Roberto Romero (USA), Yves Ville (France) and Gerry Visser (Netherlands) among many others. As is customary, cutting-edge research and the latest hot topics in fetal medicine were discussed during the congress.

On Sunday, the sessions addressed various lung and brain abnormalities. In addition, there was an interesting discussion on spina bifida and fetal anemia. It all culminated in a session on fetal growth restriction and the delegates subsequently attended the welcome party at the end of the first day which was held at Ljubljana’s Convention and Exhibition Center.

Day two, Monday, commenced with various discussions on placental abnormalities. This was followed by a session on twin complications during pregnancy. Finally, the day ended with a specific session highlighting the importance and clinical utility of cfDNA in pregnancy. Tuesday was cardiac day by excellence. It was led by luminaries in the field at the forefront of whom were Rabih Chaoui (Germany), Marrietta Charakida (UK) and Vita Zidere (UK). They gave outstanding comprehensive talks and presented most interesting cases depicting different fetal cardiac defects. There was also a session on the prediction and prevention of preterm birth. Again, the delegates were all invited to a special dinner party hosted by Professor Nicolaidis that took everyone back in time with a special vintage theme represented by old wooden chairs and tables that were spread across the ballroom. Everyone enjoyed hours of dancing to old 70’s songs that were being played by a live band. One of the congress’ major highlights was the presentation of the ASPRE study outcomes. The results were presented by Liona Poon (Hong Kong) on Wednesday the 28<sup>th</sup> of June and the findings were simultaneously published in the online issue of the New England Journal of Medicine. The trial started at King’s College Hospital in the United Kingdom in April 2014 and recruitment was completed in April 2016. Around 1600 women completed the double-blinded placebo-controlled study. Just short of 800 women were randomly allocated into daily 150 mg of aspirin, while just over 800 women were allocated to the placebo group. The women were recruited at 13 different maternity hospitals across Europe. The high risk group of women for the development of pre-eclampsia was identified according to their mean arterial pressure, resistivity index of the uterine arteries, biochemical markers, and maternal risk factors. Administration of 150 mg of aspirin daily to the high risk group, from 11-14 weeks up until 36 weeks, resulted in a significant reduction in risk of developing pre-term pre-eclampsia. The study shall undoubtedly open a new era in the prevention pre-eclampsia, one of the most morbid conditions in pregnancy. Thursday was the last day in the congress. It commenced with a session on maternal fetal diseases and various infections contracted during pregnancy that could cause serious fetal morbidities such as CMV and Zika virus. In addition, there were sessions dedicated to labor and delivery and the predictors of successful induction of labor. The congress ended with a trip to Bled, a lake in Slovenia with an amazing landscape where all the delegates got the chance to mingle, enjoy the natural beauty and reflect back on 5 amazing days. Stay tuned to the **FMF Website** for details on next year’s congress.



Professor Nicolaidis



Professors Bilardo &amp; Visser with Delegates

## Highlights from “Fetal Care in Saudi Arabia Status and Future” Held May 10 - 11, 2017 at King Faisal Specialist Hospital and Research Center in Riyadh, SA

**King Faisal Specialist Hospital and Research Center (KFSHRC)** held its first “Fetal Care” symposium in Riyadh this past May. The symposium included international leaders in fetal medicine, at the forefront of which were Drs. Polzin and Peiro from the **Cincinnati Fetal Care Center** and **Cincinnati Children’s Hospital**, in addition to the esteemed fetal care team at KFSHRC who gathered for 2 days to learn about the latest advances in fetal medicine as well as get an overview of the amazing accomplishments at the Fetal Care Center at KFSHRC.

The conference’s attendees came from all over the Kingdom of Saudi Arabia. Given the nature of the symposium, there were fetal medicine specialists in addition to geneticists, pediatric cardiologists, pediatric surgeons as well as neonatologists. Each brought unique expertise and vision. This enabled the symposium to offer a comprehensive and holistic approach to the most frequently encountered and treatable fetal conditions.

Day one commenced with a morning keynote lecture on the latest innovations in the in-utero treatment of spina bifida by Dr. Peiro who reviewed the experience in Cincinnati. Dr. Polzin then gave an overview on prenatal management of lower urinary tract obstruction with a special concentration on the Cincinnati experience. Dr. Peiro then discussed congenital diaphragmatic hernia and Dr. Polzin discussed the amniopore for amniotic fluid replacement. This was followed by a session on genetics and the pioneering work being carried out at KFSHRC under the leadership of Dr. Fowzan Alkuraya. The afternoon’s first session was dedicated to the fetal heart where various topics were discussed such as latest markers and trends in screening for congenital heart defects, fetal arrhythmias, and balloon aortic valvuloplasty. The lectures were given by Drs. Almugbel and Khan among others. Dr. Khan gave an outstanding presentation on the diagnosis, management and outcome of fetuses with congenital heart defects at KFSHRC. Day two commenced with a brilliant morning keynote lecture given by Dr. Polzin on fetal therapy for monochorionic twin gestations. The complex topic was delivered in the simplest most comprehensible style where decades of invaluable practical clinical experience were shared with the attendees in mere 45 minutes. Dr. Alshanafeey then presented the experience at KFSHRC and the tremendous impact the team has had on the outcome of the fetuses of these complicated gestation: truly commendable work! The challenging topics of when and how to intervene for selective FGR and TRAP, and the local experience, were then reviewed by Drs. Kateb, Tulbah and Alnemer. Dr. Kurdi presented personal experience with the difficult topic of selective fetal reduction. Dr. Alsaah presented the local experience with invasive procedures, and Dr. Almubarak presented KFSHRC’s experience with in-utero fetal transfusions. The final session concluded with a captivating presentation by Dr. Peiro on fetoscopic surgery for amniotic band syndrome. The symposium culminated with a critical discussion on the ethical issues and family’s perspectives on fetal interventions.

Indeed, this proved to be a most memorable symposium where knowledge was exchanged at the highest possible level in such a welcoming and friendly set up. The work that is being done at the KFSHRC truly serves as a role model for us in the Middle East. Our national societies should prioritize and encourage close collaboration amongst our nations in order to facilitate the exchange of knowledge and expertise, and positively impact the outcome of our future generations...



W. Polzin, MD



J. Peiro, MD



R. Khan, MD

# CF AFC Recommends ISUOG's Updated Consensus Statement on the Impact of cfDNA Aneuploidy Testing

The new updated **consensus statement** has been issued by **ISUOG** addressing the impact of cfDNA aneuploidy testing on screening policies and prenatal ultrasound practices. The statement reaffirms the persisting role of prenatal ultrasound in view of the widespread availability and utilization of cfDNA testing.

Some of the key points highlighted in the consensus statement are that:

- All women should undergo a first trimester scan, in accordance with **ISUOG's First Trimester Guidelines**, irrespective of their decision to undergo cfDNA testing
- The a-priori risk as well as fetal cell fraction are crucial in the interpretation of cfDNA testing results
- In case of a structural abnormality, the indications for invasive testing/microarrays should not be affected by a prior negative cfDNA test
- Patients should be provided with proper counseling stressing the fact that cfDNA testing is a screening not a diagnostic test
- Accuracy of cfDNA testing in twins is in need of further validation
- With the possibility to test for certain microdeletions, it is important to note the accompanying increase in false positive and failure rates

The consensus statement concludes by stressing the fact that we are in urgent need of further prospective publicly-funded studies in order to determine the cost effectiveness of the various screening modalities available to us today.



## THIS AND THAT

### AIUM Abstract Submission



Abstract submission is open for the **AIUM Annual Convention** to be held in NY March 24-28, 2018. The convention has been redesigned with a new most exciting format and will include comprehensive pre-congress courses, cutting edge research, "learning Labs", "meet the professor" sessions and special interest tracks. There is something for everyone: from the student to the most advanced. Details at the **AIUM Website**.

### Upcoming ISUOG Activities



**ISUOG's 27th World Congress** will be held in Vienna on Sept 16-19 with special pre-congress courses on the 15th. It will be another trend-setting congress with world leaders exchanging the latest that technology has to offer with the opportunity to attend live-scanning sessions, workshops and interactive hubs. The Basic Training course will be live-streamed for those who cannot attend. For more information, visit the **ISUOG Website**.

### Upcoming LSOG



The **21st International Annual Congress of LSOG** will be held Nov 9-11 in Beirut. The scientific committee has put together an outstanding program to be delivered by such luminaries as Drs. Wapner, Thornton and Saade in addition to other regional and national experts. There will be 5 pre-congress workshops addressing various topics among which are obstetric interventions and recurrent pregnancy loss. Details at the **LSOG Website**.

### Fetal Heart Society



The **Fetal Heart Society** is a non-profit organization established in 2014 with the goal to advance the field of fetal cardiovascular care and science through collaborative research, education and mentorship. Membership is open to fetal care specialists across all disciplines including pediatric cardiology, obstetrics, and other relevant subspecialties. The society welcomes physicians, nurses, sonographers, researchers, and trainees with an interest in fetal cardiovascular medicine. Until recently, membership was limited to professionals in North America, though in 2017 membership was expanded to include a limited number of international professionals. For more details, visit the **FHS website**. If you practice outside of North America and are interested in joining, please contact [membership@fetalheartsociety.org](mailto:membership@fetalheartsociety.org)

### CF AFC News



This quarter, **CF AFC's** Reem S. Abu-Rustum was invited as a speaker at the **KFSHRC** Fetal Care Symposium in Riyadh, served as Co-Director/Speaker at **ISUOG** Masterclasses and Co-Chair/Speaker at **ISUOG BT** Course at **EBCOG** in Antalya. She chaired **ISUOG's** BT Summit in London and was invited to present an **AIUM Webinar**. She was a speaker at the **UF Ob/Gyn** Resident/Fellow Graduation & Alumni Reunion Meeting in Florida. She was appointed a member of the **FHS** Education Committee, and co-authored an **AIUM Case Challenge**. She is ever so grateful for all the opportunities...

### Hot-Off-The-Press: Outcome of Fetal Ovarian Cysts

*Ultrasound Obstet Gynecol* 2017; 50: 20-31  
Published online 7 June 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uoq.16002

#### Outcome of fetal ovarian cysts diagnosed on prenatal ultrasound examination: systematic review and meta-analysis

F. BASCIETTO<sup>1</sup>, M. LIBERATI<sup>1</sup>, L. MARRONE<sup>1</sup>, A. KHALIL<sup>2</sup>, G. PAGANI<sup>3</sup>, S. GUSTAPANE<sup>1</sup>, M. LEOMBRONI<sup>1</sup>, D. BUCA<sup>1</sup>, M. E. FLACCO<sup>4</sup>, G. RIZZO<sup>5</sup>, G. ACHARYA<sup>6,7</sup>, L. MANZOLI<sup>4</sup> and F. D'ANTONIO<sup>6,7</sup>

Bascietto et al recently published a systemic review and meta-analysis in **UOG** on the outcome of prenatally-diagnosed fetal ovarian cysts. This is a concerning finding, for both patients and families, as to its implications and prognosis.



Sagittal view of a Hemorrhagic Cyst

Concerns vary across cultures and there may be much worry as to how a prenatally diagnosed ovarian cyst may ultimately affect the unborn baby's reproductive potential.



Axial View of a Hemorrhagic Cyst

In their review, the authors evaluated 34 studies which included 954 fetuses. The key end points that they assessed were: the rate of cyst resolution, the change in the cyst's appearance, the risk for torsion, the risk for post-natal surgery, need for oophorectomy, and the accuracy of ultrasound among others.

The study's main findings were affected by whether or not the cyst size was greater or less than 4cm. When the cyst was found to be larger than 4 cm prenatally, then the chances for resolution were less, the likelihood of torsion was higher and so was the need for postnatal surgery. As to the cyst appearance, whenever the cyst had a complex appearance then the chances for resolution were lower and the likelihood of having postnatal surgery were higher, irrespective of the cyst size. The authors could not arrive at any robust conclusions pertaining to the utility of in-utero aspiration and they call for randomized and properly powered studies in order to obtain evidence-based results on the role of in-utero therapy.

The authors conclude that whenever a cyst is diagnosed, sonographic surveillance is the most reasonable and safest option to monitor the cyst size and any changes in its complexity. They caution that the optimal management of these fetuses remains controversial, and that the clinician needs to try and avoid iatrogenic pre-term delivery.



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CFAFC expresses its sincerest appreciation to all of our contributors. A special thank you to Prof. Katia Bilardo for the inspiration... For any interesting cases, comments, suggestions or special announcements, e-mail [rar@cfafc.org](mailto:rar@cfafc.org)

**“If it isn’t a passion,  
It isn’t burning,  
It isn’t on fire,  
You haven’t lived”.**  
*Diana Vreeland*

Kindly note that all colored text contains embedded **“clickable”** links.

## SANA Medical NGO and Hopital Aboujaoude Commence “Basic Training in Ob/Gyn US”

**SANA** and **Hopital Aboujaoude** commenced the first Resident Training Course in Ob/Gyn Ultrasound in cooperation with **ISUOG**, and structured in accordance with **ISUOG BT** (Basic Training) Guidelines in April. This is the first such endeavor and shall hopefully pave the way to a National Standardized Curriculum in Ob/Gyn Ultrasound Training for our Ob/Gyn and Radiology residents here in Lebanon. This has been the result of rigorous work and planning over 10 months between our Lebanon team and ISUOG. We have 10 junior residents, all in their first 2 years of residency, from both Ob/Gyn and Radiology residency programs, at the Lebanese University and the University of Balamand, selected for our “pilot” course. Over the course of 2017, there shall be monthly sessions of didactic as well as simulation-based training. Our core faculty are: Drs. Aboujaoude, Abu-Rustum, Daou and Helou. The residents have an intensive course planned with both a theoretical and a practical component. There shall be online learning, log book up-keep and hands-on training with strict adherence to pre-set metrics to ensure competency requirements are met in the submitted images. Upon successful completion of all requirements, there shall be certification. Thank you **ISUOG**, as always, for the endless opportunities...



The Lebanon Team



A Lecture by Prof. Tabor



The Course Manual

## Upcoming Congresses

COURSE TITLE	DATES	LOCATION	WEBSITE ADDRESS
2nd Annual Fetal Symposium on the Fetal Brain	Aug 24 - 25, 2017	Washington, DC	<a href="http://www.fetalbrainsymposium.com">http://www.fetalbrainsymposium.com</a>
4th International Meeting FNPS 2017	Sep 2 - 5, 2017	Osaka, Japan	<a href="http://www.c-linkage.co.jp/fnps2017/">http://www.c-linkage.co.jp/fnps2017/</a>
Fetal and Women’s Imaging: Advanced Ob-Gyn Ultrasound	Sep 8 - 10, 2017	Seattle, WA	<a href="http://www.worldclasscme.com/conferences/fetal-and-womens-imaging-advanced-ob-gyn-ultrasound2/">http://www.worldclasscme.com/conferences/fetal-and-womens-imaging-advanced-ob-gyn-ultrasound2/</a>
27th World Congress on Ultrasound in Obstetrics and Gynecology	Sep 16 - 19, 2017	Vienna, Austria	<a href="http://www.isuog.org/WorldCongress/2017">http://www.isuog.org/WorldCongress/2017</a>
6th International Conference on Fetal Growth	Sep 20 - 22, 2017	Cork, Ireland	<a href="http://www.fetalgrowth.org">http://www.fetalgrowth.org</a>
8th Annual Fetal Echocardiography: Normal and Abnormal Hearts	Oct 5 - 7, 2017	Las Vegas, NV	<a href="http://www.edusymp.com/product/details/999">http://www.edusymp.com/product/details/999</a>
7th Annual Fetal Echocardiography Symposium at UCLA	Oct 21, 2017	Los Angeles, CA	<a href="http://www.cme.ucla.edu/courses/event-description?registration_id=169414">http://www.cme.ucla.edu/courses/event-description?registration_id=169414</a>
Advances in Fetology 2017	Oct 27 - 28, 2017	Cincinnati, OH	<a href="https://cchmc.cloud-cme.com/aph.aspx?P=5&amp;EID=20484#">https://cchmc.cloud-cme.com/aph.aspx?P=5&amp;EID=20484#</a>
The 8th Phoenix Fetal Cardiology Symposium	Oct 27- 31, 2017	Phoenix, AZ	<a href="http://www.fetalcardio.com">http://www.fetalcardio.com</a>
21st International Congress of the Lebanese Society of Ob/Gyn	Nov 9 - 11, 2017	Beirut, Lebanon	<a href="http://lsog2017.com">http://lsog2017.com</a>