



# Center For Advanced Fetal Care Newsletter

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## The Millinneals...

...are everywhere: they are our children, our students and our patients. They are e-savvy with such a sense of entitlement, coming to our clinics having already diagnosed themselves, making demands as to workups and surgical procedures, with such defiance and unwillingness to adhere to all that is traditional. It is even a greater challenge to mentor and teach them, those future doctors, with the wealth of information they carry on their smart phones, and the technological advances that are available to them, enabling them to diagnose much earlier in their careers, and with such greater confidence. And it was so perfectly described by Mark Anderson, a millinneeal, on Digital Learners that: "For the first time in history, we are no longer limited by our teachers' ability and knowledge". This futuristic generation that shall inherit our world, rule it, and ultimately doctor us, has been described as narcissistic, egotistical and selfish (Time 20 May 2013). Yet at the same time, they are "evolution in progress", re-shaping the world we live in and re-defining our standards and guidelines. As such, we dedicate this issue to the "millinneals", students and patients, as we shed light on what lies ahead to help us, pre-millinneals, properly doctor and train these futuristic minds. We present Bianchi's brilliantly laid-down foundations for the in-utero treatment of Trisomy 21 fetuses. We present highlights from the trend-setting FMF's 12th World Congress. We present the latest on non-invasive prenatal diagnosis which eventually the millinneeal patients, in their quest for maximal reassurance as to the future health of their offspring, shall force regulating bodies to mandate routine non-invasive prenatal testing, soon be followed by whole genome sequencing from maternal blood. For our quarterly feature for 2013: Year of Ultrasound, we present the Middle East's first experience with ultrasound in medical education, in addition to our usual features. We hope that with this "millinneeal" issue we may clarify what seems unclear today to avoid fear of our medical tomorrow, in tune with what the Man of Steel said in this summer's hit movie Superman: "People are afraid of what they don't understand". In addition, we hope to call out to those resisting change, echoing his father's words to him: "You will give the people an ideal to strive towards. They will race behind you, they will stumble, they will fall. But in time, they will join you in the sun. In time, you will help them accomplish wonders".



Time 20 May 2013



Time 20 May 2013

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## NIPT: Opportunity for Antenatal Treatment of Down Syndrome?

Brilliant vision and futurism is how one would describe the latest review by Guedj & Bianchi (Prenatal Diagnosis 2013; 33: 614-618) in which they state that with today's current advances, especially with the global availability of non-invasive prenatal testing (NIPT) and the ability to screen for Trisomy 21 starting at 10 weeks of gestation, we now have a golden opportunity to potentially commence in-utero treatment on those fetuses to impact their neurodevelopmental outcome. Evidence from various molecular, cellular and morphogenetic studies is presented in support of the notion that with antenatal intervention both the neurocognition and the behavior of those affected fetuses may be improved. The families would then have an option besides today's mere option of continuation or interruption of the pregnancy. Results on in-utero treatment of the mouse model with apigenin, which has the potential of decreasing antioxidative stress, are discussed, and apigenin's positive impact on the postnatal exploratory behavior of those pups is presented. Bianchi gave a most compelling presentation at the 12th World Congress of the Fetal Medicine Foundation in Marbella 24 June 2013 which can be viewed (on a desktop/laptop) by clicking [Professor Bianchi at FMF 2013](#).



Professor Bianchi at FMF

## 2nd Generation NIPT: Can It Replace Invasive Testing?

Reported sensitivities of non-invasive prenatal testing (NIPT) are > 99% for Trisomy 21, 97% for Trisomy 18 and 80% for Trisomy 13. Confirmation by invasive testing remains a must. This has been largely attributed to guanine-cytosine (GC) bias. In the newest report by Guex et al (Prenatal Diagnosis 2013; 33: 1-4) on a total of 276 cases (107 aneuploid and 169 euploid), a 2nd generation NIPT was used. Here, a genome-wide test for fetal aneuploidy based on shotgun sequencing cell-free DNA in maternal blood was utilized where all individual steps were optimized, rigorous quality control was carried out, GC bias was removed, robust detection of fetal DNA fraction was achieved, with appropriately powered counting metrics. Guex et al were able to achieve sensitivities and specificities of 100% for Trisomy 21, 13, 16, 22, 45,X and 47,XXX, and those were 95.8% and 100% for Trisomy 18. As such, with 2nd generation NIPT, invasive testing may soon be obsolete...

## Highlights from the 12th World Congress of the Fetal Medicine Foundation Held From 23 - 27 June 2013 in Marbella - Spain

It was under the effects of a “super moon” that the 12th World Congress of the Fetal Medicine Foundation was held. It was indeed a full house with over 2000 delegates from 87 countries hypnotized and glued to their chairs, over 5 intensely packed 12-hour days, in the picturesque Marbella, Spain. The level of interaction, the energy and the intensity were clearly reflective of a “super moon”!

The congress commenced with the Eurofet sessions in which extensive coverage of the postnatal outcome on fetuses with abdominal wall defects, esophageal atresia, diaphragmatic hernias and spina bifida was carried out. However, Professor Di Coppi's presentation on tissue engineering in the perinatal period was the absolute highlight addressing the futuristic utilization of decellularized tissue as the model from which to obtain the tissue 'architecture' in order to regenerate intestinal, hepatic, renal and pulmonary tissue. Professor Di Coppi presented data on rat, pig as well as sheep models, together with experience with a human trachea. He successfully relayed that tissue engineering, despite major obstacles, is the answer and has such great promise for the future treatment of babies with congenital abnormalities.

Professor Nicolaides presented the “millinial” inverted pyramid of antenatal care incorporating the latest modalities of screening, namely non-invasive prenatal testing (NIPT). He predicted the continued screening adjustments as we evolve and advance with NIPT, yet he stressed the continued critical and irreplaceable role of the first trimester scan in the screening and early detection of structural fetal abnormalities. Professor Lewi presented a wonderful overview on the various types of placentation of monozygotic twins, which she artistically displayed having injected numerous placentas with color-coded ink to depict all the anastomoses whether arteriovenous or not. She reported that in only 5% of monozygotic twins are there no anastomoses. Professor Chaoui gave a memorable most informative presentation on anomalous pulmonary venous return with absolutely stunning images. Professor Allan gave an overview of her personal experience with prenatal diagnosis of congenital heart disease over many decades, culminating in her announcing her retirement, via a touching video clip, which brought the entire crowd to its feet for a lengthy standing ovation! The Jani group from Belgium was as distinguished as ever with two beautifully illustrated novel presentations. The first, presented by Professor Jani, addressed the latest pertaining to MR imaging of the abdomen in cases of maternal acute abdomen, abnormal placentation (accreta/percreta/increta), uterine scar dehiscence, ectopic pregnancy among several other diagnoses. He stressed the role of ultrasound first with an additive role of MR especially in suspected cases of appendicitis. The second was by Dr. Carmela Votino in which she presented a novel approach to virtual autopsy using post mortem sonography on over 100 fetuses throughout gestation scanned after birth. Volume data sets were obtained for off-line review by a second observer, and findings were confirmed by autopsy. The images displayed were outstanding and the value of the virtual autopsy proved to be additive and correlated highly with findings at autopsy. A most interesting, educational interactive session, with audience participation, was presented by Professors Christoph Berg, Annegret Geipel and Oliver Kagan from Germany together with UK's Asma Khalil, on fetal surgical anomalies with discussions on the latest in the management of some very challenging cases.

Lebanon was well represented this year at the congress with one oral presentation and 10 poster presentations. This was the collaborative effort of 21 colleagues from all over the country namely: A. Abdelahad, R. Abu-Rustum, S. Abu-Rustum, C. Afif, H. Attallah, T. Atta, E. Attieh, R. Bassil, S. Chalhoub, A. Daher, L. Daher, D. Elia, R. Fahed, A. Frangieh, W. Jreige, G. Kehdy, A. Kesrouani, B. Nasr, E. Sneider, B. Soutou and F. Ziade. It certainly was wonderful to see the results of unified fruitful collaboration.

And with that we end our report on yet another trend-setting Nicolaides Congress, and we now commence the countdown to next year's congress. Details on the 13th World Congress will post to the [FMF website](#) in the near future...



## ISUOG's “Early Pregnancy Care and Acute Gynecology Course Series” 16 - 17 June 2013 at the New ISUOG Offices, London

ISUOG was delighted to welcome delegates from 14 different countries to London to attend the “Early Pregnancy Care and Acute Gynecology Course Series” for the very first time held at the new ISUOG offices. With a dedicated space just for interactive, small group hands-on programs, ISUOG's new education space aims to be a pioneering, visionary hub of knowledge and training in the use of ultrasound in Obstetrics and Gynecology. Chaired by Professor Tom Bourne, faculty and delegates enjoyed a varied program that included case examples and just image sessions on a number of topics such as viable pregnancies, the use of power Doppler, miscarriage, ectopic pregnancy and the management of women

who present with pain and bleeding. Plenty of case examples and practical recommendations allowed for great speaker and delegate interaction throughout. For more information on all of ISUOG's upcoming events and courses, please visit the ISUOG website on a regular basis by clicking on the following link: [ISUOG Courses](#).



With ISUOG Permission

## Quarterly Feature 2013:YOU...University of Balamand's Faculty of Medicine Pioneers Ultrasound in Med Ed in the Middle East



The momentum of 2013: Year of Ultrasound has now travelled across the globe to the Middle East, and has landed at the University of Balamand (UOB) in Lebanon where Camille Nassar, PhD, Dean of the medical school, has taken the pioneering step of introducing ultrasound into the curriculum of the first year medical students. The students at UOB had their first taste of ultrasound over a 6 week period at the end of their first year of medical education. The course constituted of didactic as well as hands on sessions. The students rated this experience as the highlight of their year and here are some of the students remarks at the completion of the course:

1- Amazing course!! Most favorite part of Med 1; 2- Great course; 3- Such an amazing course/should be integrated throughout the coming years. Best course in Med 1; 4- The experience has truly enriched my interest in clinical practice. I believe it has given us a glimpse into what we will be doing in the future and I would love to teach the upcoming Med 1 Classes; 5- I strongly advise the integration of ultrasound in all med classes because it is crucial to train our eyes for several years to be professional clinicians. Thus several years of ultrasound course are definitely better than just 1 or 2 years in Med 1 and Med 2; 6- Great course, I hope we continue with throughout our med years; 7- It gave me, at least a feel for the machine, which is beneficial for future experience; 8- Give together with the anatomy lab. This was the most useful and interesting clinical experience.

With this most encouraging feedback, Dean Nassar has future plans currently underway for a fully-integrated 4 year curriculum. The faculty at UOB wish to express their sincerest appreciation to the Society of Ultrasound in Medical Education (SUSME) for serving as the true inspiration, and to thank SUSME for its online free modules that were instrumental for the success of the course. Further details on upcoming related activities on ultrasound in medical education are available at the following websites: [2013:YOU](#), [SUSME](#) and [WCUME](#).

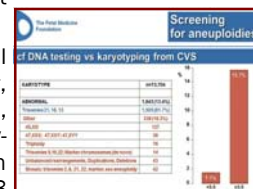
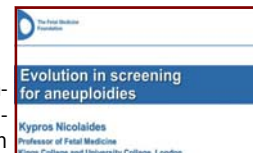


## CFAFC's Recommendation: Nicolaides' Webinar

From the mastermind behind first trimester screening comes an online webinar on the "Evolution in Screening for Aneuploidies" available at [Professor Nicolaides on the evolution of screening](#). Professor Nicolaides discusses the evolution of all forms of prenatal diagnosis from maternal age, to invasive procedures, to first and second trimester serum biochemistry, to the nuchal translucency (NT), to various other first trimester markers, culminating with the recent introduction of non-invasive prenatal testing utilizing cell free fetal DNA in the maternal circulation (NIPT).

Highlights from the webinar include whom should we offer NIPT to and Nicolaides calls for generalized screening of all women utilizing NIPT with its greater than 99% sensitivity for Trisomy 21 at a false positive rate of < 0.01%. However, since today NIPT is limited to the trisomies, whenever there is a high index of suspicion for an underlying syndrome, then invasive testing needs to be carried out and microarrays need to be utilized as indicated. And based on fetal karyotyping by CVS on 13704 fetuses at the Fetal Medicine Foundation, it was found that whenever the NT is > 3.5 then there is a much higher chance (15.7% vs 1.5%) for the fetus to be affected by something other than Trisomy 21, 18 and 13, and in those cases, it is in the patient's best interest to perform invasive testing. In addition, Nicolaides explains the differences in the current NIPT techniques, the concept of fetal cell fraction and how it is affected by both maternal weight and placental mass, and he presents data in support of its applicability in the low risk population.

Nicolaides concludes that NIPT is the safest, most effective screening modality available to women to date, nonetheless, cost is the main limiting factor. Nicolaides closes by urging worldwide governing bodies to make NIPT available to all women, irrespective of age and risk, hoping that its global implementation shall proceed at a much higher rate than the 20 years it took for NT implementation...



Screening Method	Trisomy 21	Trisomy 18	Trisomy 13
First Trimester Screening	85%	75%	70%
Second Trimester Screening	80%	70%	65%
Combined First and Second Trimester Screening	92%	85%	80%
NIPT	99%	99%	99%

## THIS AND THAT

### AIUM Abstract Submission



Abstract submission for the annual Convention of the AIUM is now open at [AIUM 2014 Abstract Submission](#) till 26 September 2013. Abstracts may be submitted for consideration as e-posters or oral communication. This year's convention will be held in Las Vegas 29 March to 2 April, 2014 and promises to build on the success of the preceding conventions.

### Upcoming Congress ISUOG



The 23<sup>rd</sup> ISUOG Annual Congress will be held in conjunction with ASUM 43<sup>rd</sup> Annual Scientific Meeting, in Sydney, Australia on 6-9 October 2013. The Pre-Congress Courses will take place on Saturday, 5 October 2013 on the topics of prenatal diagnosis, endometriosis and ultrasound in the O&G office. The Congress' scientific program will focus on parallel streams by sub-speciality to showcase state of the art updates and new research presentations in obstetrics, gynecology, pediatrics, MSK and vascular ultrasound. Registration and further information on this annual event is available on the [ISUOG website](#).

### SUSME's



It has been a little over 2 years since the landmark 1st WCUME by the Society of Ultrasound in Medical Education was held in Columbia, South Carolina and it is with much excitement that we announce that the 2nd WCUME is coming back to Columbia where it is being hosted by the University of South Carolina as an official designated 2013: Year of Ultrasound event. A wealth of plenary sessions and hands on workshops are planned with such world leaders in the field as SUSME's President Michael Blaivas, MD, the University of South Carolina's Dean Richard Hoppmann, MD and Ohio's David Bahner, MD to name a few. For detailed information and online registration please visit the [WCUME website](#).

### New on Twitter: Journal of Ultrasound in Medicine



Follow the Journal of Ultrasound in Medicine on Twitter: @jultrasoundmed to stay updated on its latest news, upcoming issue content, and in order to gain access to the latest AIUM Guidelines and the Sound Judgement Series in support of Ultrasound First. In addition, JUM welcomes the views and recommendations of its readership.

### Upcoming Annual Congress of LSOG



As has become customary every fall, the Lebanese Society of Ob/Gyn is planning its annual convention at the Movenpick in Beirut November 14-16 with several pre-congress workshops as well as a comprehensive program given by local and international speakers. For further information, please visit [LSOG 2013](#).

## Hot-Off-The-Press: The prefrontal space ratio in 2nd & 3rd Trimester Screening for Trisomy 21. Yazdi et al, UOG 2013; 41: 262-266

Further evidence as to the importance of evaluating the fetal profile in the second and third trimesters of pregnancy in the screening for Trisomy 21 was published recently in the white journal.

This was a retrospective study from Germany carried out on 279 euploid fetuses and 81 fetuses with Trisomy 21 on whom stored volume data sets were retrieved and from which the mid-sagittal plane was generated. For the normal fetuses, a line was drawn from the leading edge of the mandible to the leading edge of the maxilla and was extended in front of the fetal forehead (MM line). Subsequently the prefrontal space ratio (PFSR) was calculated as the ratio d2/d1 where d1 is the distance from the leading edge of the skull to the leading edge of the skin, and d2 is the distance d2 from the leading edge of the skin to the MM line (Figure 1). Using multiple regression analysis demonstrated that the PFSR was independent of both the maternal and gestational age.



Figure 1

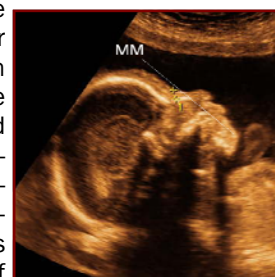


Figure 2

In euploid fetuses, the PFSR is 0.97. However in Trisomy 21 fetuses, there is an increase in the prefrontal space (Figure 2) and hence an increase in d1. This results in a decrease in the PFSR. As such, in Trisomy 21 fetuses, the PFSR decreases to 0.2 (P<0.0001). In this study, the PFSR was below the 5th centile in only 4.7% of euploid fetuses versus in 79.1% of fetuses with Trisomy 21.

The authors conclude the obtaining the MM line and measuring the PFSR is a simple measurement to obtain, and that it is an effective second and third trimester marker for trisomy 21.



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[Click Here For Full Free Access To Prenatal Diagnosis June 2013](#)

For any interesting case reports, comments, suggestions or announcements to be included in our newsletter, please send an e-mail to [rar@cfafc.org](mailto:rar@cfafc.org).

## Prenatal Diagnosis of Coarctation of the Aorta. Case by Mohamad Abdalkader MD, Nabil Helou MD & Linda Daou MD.

A 28 yo G1PO with a negative past history and normal first and second trimester scans presented for a third trimester scan at 34 weeks. The third trimester scan was notable for ventricular disproportion (VD) with the right ventricle larger than the left (Figure 1). In addition, the pulmonary artery (PA) (Figure 2) was larger, 7.1 mm, than the aorta (Ao) (Figure 3), 4.5 mm, with a PA/Ao of 1.6. A dilated ductal arch, a narrowed aortic arch and a contraductal shelf were visualized (Figure 4). Otherwise, there was normal flow across the mitral and tricuspid valves and the pulmonary veins were seen inserting into the left atrium. Peak systolic velocities (PSV) were normal across the pulmonic valve. However, PSV was in excess of 200 cm/sec for the aortic valve. Consultation with our pediatric cardiologist confirmed the primary suspicion of underlying coarctation.

Prenatal diagnosis of coarctation of the aorta remains a challenge. However, it is a critical diagnosis to make in order to improve the neonatal outcome of these babies. Echocardiography has low sensitivity and specificity, but it plays a major role in identifying the at risk groups. Several markers have been described to improve the prenatal detection of coarctation, at the forefront of which is VD. However, VD is non-specific and if isolated, may lead to unnecessary precautions and undue parental anxiety in 80% of cases especially in the 3<sup>rd</sup> trimester when developmentally, the right ventricle is larger than the left. Another sensitive prenatal marker for coarctation is a PA/Ao > 1.6, as was found in our case.

In summary, VD on prenatal sonography may be a sign of underlying congenital heart disease and warrants careful fetal and neonatal follow-up. This is especially applicable in cases where there is asymmetry in the outflow tracts with a PA/Ao > 1.6. Caution is critical in order to properly identify the at risk fetuses yet avoid undue parental anxiety.

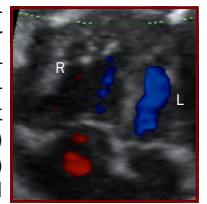


Figure 1

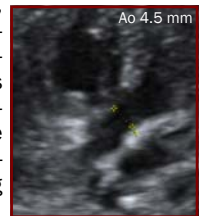


Figure 2



Figure 3



Figure 4

## Upcoming Congresses

COURSE TITLE	DATES	LOCATION	WEBSITE ADDRESS
2nd International Conference on Fetal Growth	September 19-21, 2013	Baltimore, MA	<a href="http://www.fetalgrowth.org">www.fetalgrowth.org</a>
2nd World Congress of Ultrasound in Medical Education	September 27-29, 2013	Columbia, SC	<a href="http://www.wcume.org/about/conference-program/">www.wcume.org/about/conference-program/</a>
1st FIGO Africa Regional Conference of Gynecology & Obstetrics	October 2-5, 2013	Addis Ababa, Ethiopia	<a href="http://www.comtecmed.com/figoafrika/default.aspx">www.comtecmed.com/figoafrika/default.aspx</a>
ISUOG's 23rd World Congress	October 6-9, 2013	Sydney, Australia	<a href="http://www.isuog.org/WorldCongress/2013/">www.isuog.org/WorldCongress/2013/</a>
25th Congress of the European Federation of Societies for Ultrasound in Medicine & Biology	October 9-12, 2013	Stuttgart, Germany	<a href="http://www.euroson2013.org/general-information.html">www.euroson2013.org/general-information.html</a>
National Conference on Ob/Gyn Ultrasound	October 18-20, 2013	Atlanta, GA	<a href="http://www.iame.com/conferences/ob16/#program">www.iame.com/conferences/ob16/#program</a>
3rd Annual Fetal Echo Symposium at UCLA	October 19, 2013	Los Angeles, CA	<a href="http://www.cme.ucla.edu/courses/event-description?event%5fid=2101400">www.cme.ucla.edu/courses/event-description?event%5fid=2101400</a>
4th Annual Fetal Echocardiography: Normal and Abnormal Hearts	October 25-26, 2013	Las Vegas, NV	<a href="http://www.edusymp.com/product/details/580">www.edusymp.com/product/details/580</a>
Obstetric Ultrasound in the High Risk Patient	November 1-3, 2013	Las Vegas, NV	<a href="http://www.iame.com/conferences/hr14/">www.iame.com/conferences/hr14/</a>
Annual Congress of the Lebanese Society of Obstetrics & Gynecology	November 14-16, 2013	Beirut, Lebanon	<a href="http://www.lsog.2013.com">www.lsog.2013.com</a>
7eme Congres de Medecine Foetale	November 25-27, 2013	Montpellier, France	<a href="http://www.congres-medecinefoetale.fr/PROGRAMME_a22.html">www.congres-medecinefoetale.fr/PROGRAMME_a22.html</a>