International Academy of Perinatal Medicine
Report on IAPM activities in a period May 2018 – May 2019
To remind you....

In February 2017 we had annual meeting in KHARTOUM - SUDAN
13th meeting of

INTERNATIONAL ACADEMY OF PERINATAL MEDICINE

17-19 February 2017 – Khartoum (Sudan)

Venue: Police Conference Centre

Friday, 17th February
Administrative and Ceremonial meeting

Saturday, 18th February

Scientific Symposium
Recent Advances in Perinatal Medicine
Under The Patronage of His Excellency
The Sudan vice President Bakrie Hassan Salih
Report on IAPM activities in a period May 2018 – May 2019
14th INTERNATIONAL ACADEMY OF PERINATAL MEDICINE CONFERENCE
34th FETUS AS A PATIENT INTERNATIONAL CONGRESS

17-19 May
Bucharest
ROMANIA

2018

www.fetus2018.eu

Program
Administrative and Ceremonial meeting

Ghica Palace Bucharest
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Miroslaw Wielgos
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Vedran Stefanovic
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1. Themistoklis I. Dagklis, Greece
2. Josip Juras, Croatia
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4. Panos Antsaklis, Greece
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PAPERS PUBLISHED IN ACADEMY CORNER
Published in 2014

• Asim Kurjak: Global education in perinatal medicine: will the bureaucracy or smartocracy prevail? J. Perinat. Med. 2014; 42(3): 269–271

• Jose Maria Carrera: Africa is only 14 km far away from my country. J. Perinat. Med. 2014; 42(4): 427–429


Editorial

Joachim W. Dudenhauen

Academy’s Corner – a new section at JPM

The Editors and Publishers are delighted to announce a new cooperation between the International Academy of Perinatal Medicine (IAPM) and the Journal of Perinatal Medicine. From this issue, the Journal of Perinatal Medicine will become the official journal of the IAPM and will publish the Academy’s papers in the Academy’s Corner section.

The IAPM was founded in 2004 on the initiative of presidents of three scientific societies: the World Association of Perinatal Medicine (WAPM), the European Association of Perinatal Medicine (EA PM), and the International Society “The Perinatal Patient” (ISNAP). Following advice from board members of the three founding societies and from leading figures in the field of perinatal medicine, the three presidents put forward the names of candidates for election as new regular fellows. Each of the three societies elected 10 members, with the total number of regular fellows limited to 30.

On 25th May 2005, the foundation ceremony took place in Barcelona (Spain) at the Royal Academy of Medicine of Catalonia. In following years, the IAPM members have met in various capital cities all over the world, held scientific panels, and published declarations on current topics in perinatal research and patient care from a global point of view. This has been made possible by the coming together of a group of members with an exceptionally broad range of backgrounds and interests.

The aim of the IAPM is to provide a place for study, reflection, dialog, and for the promotion of perinatal medicine, especially in aspects such as bioethics, the appropriate use of technological advances, and the sociological and humanistic dimensions of the field.

The Journal of Perinatal Medicine will help the IAPM to reach these goals. It will publish the Academy’s declarations, the Academy’s papers, and other articles very quickly. The Editors of the journal hope to start the Academy’s Corner as an open forum for all members and the perinatal family. Moreover, it is safe to assume that the combined expertise of the members of IAPM will result in the journal providing an excellent resource for any obstetrician, perinatologist, and neonatologist whose practice includes pregnant women, fetuses, and newborn infants.

Joachim W. Dudenhauen

February 2014

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Academy’s Corner

Asim Kurjak

Global education in perinatal medicine: will the bureaucracy or smartocracy prevail?

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Human beings change continuously as the result of biological and cultural evolutions. Human beings change the world they live in, indeed so much so that it has been suggested that the current geopolitical epoch be named the Anthropocene epoch [6]. As knowledge now increases exponentially with a doubling time of 5-10 years, education cannot be time limited. The Millennium Development Goals state that by the year 2015 everybody should be educated [8]. Pediatric education is not an eclectic part of global education, it is its integral part. Indeed, contemporary education is education of a person that is changing and for the world that rapidly changes.

Globalization has a complex influence on perinatal health. The boards that link perinatologists together transcend geographic, political, religious, and linguistic differences, resulting in a globalization that optimizes perinatal care [2-4]. However, more than ever we need to develop education and training for physicians who provide the care and research in perinatal medicine. The USA developed its own system. The American College of Obstetrics and Gynecology is responsible for the education and practice standard. In the UK, the Royal College of Obstetricians and Gynaecologists has the unique position of providing education, developing standards, and determining how many specialists and sub-specialists are trained. In other countries, there are various levels of development and planning. The European Board and College of Obstetrics and Gynecology, for instance, are working on the accreditation of European hospitals, not only for obstetrics and gynecology standards of care, but also for setting the training and teaching roles or the subspecialties, such as maternal fetal and perinatal medicine, reproductive medicine, gynaecological oncology, and urogynecology. There is, therefore, enormous need for the advanced medical education and health care delivery systems to serve as models for developed and developing countries. To this end, the World Association of Perinatal Medicine and the International Academy of Perinatal Medicine serve as leading organizations that could become a major perinatal force for the further improvement of perinatal care throughout the developing world. Congresses of perinatal medicine in developing countries are excellent examples of how all of these ideas can be put into practice [2].

Global requirements of education

The triangle of knowledge in modern society is composed of education, research, and patients [9]. A country aspiring to a good standing in the international arena should perform well in all three corners of this triangle. Governments, universities, and firms together spend around $1.4 trillion a year on research and development, more than ever before. World trends in knowledge and virtual ideas creation demonstrate that the EU has overtaken the US in ideas creation but is still lagging behind in patents and applied ideas. Asian countries are closing the gap rapidly and the world knowledge scene is witnessing an extremely competitive and interdependent race [5].

An overview [5] of published articles in 2009 shows that the EU is still world leader in scientific articles published with 31% of the total production followed by the USA on 25.5%, China on 9.4%, with Japan on 6.5%, and South Korea on 2.8%. In the last decade, Iran and China have had fastest growth of 25% and 16%, respectively, although this was from a low base, followed by Turkey and South Korea with 10%. The EU had growth of 1.1% while the USA had 1%. When it comes to citations, in 2010, the USA was the leader with 76.4%, the EU was in second place with 12.8%, and China was in third place with 6%, followed by Japan 5.7%. This citation index, together with the well-known fact that the EU has been following the USA in number of patents for years, clearly demonstrates that transfer speed, into patents and operational and economic value, of EU articles is still lagging behind the effectiveness of the USA [9].
Academy's paper

José M. Carrera*

Africa is only 14 km away from my country

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Europe, the dream of many Africans

The concept of the “welfare state” originated in Europe. This concept ensures that despite the economic crises, citizens enjoy the benefits of high-quality national healthcare systems, education and welfare benefits that are by and large still available. Democracy also ensures that people have a right to security and a whole host of personal and collective liberties (freedom of religion, freedom of expression, etc.). It is clear that despite the current problems, the economic situation of most of its inhabitants is far better than that of most people living in Africa and Asia. This is why it is now the continent with the fewest conflicts and the longest life expectancy. The high level of maternal and infant mortality, which is a particularly well-documented aspect of health, is a clear indicator of the health of the population in Europe. The low rate of maternal mortality (less than 10 deaths per 100,000 live births), infant mortality (below 5 per 1000), and neonatal mortality (below 6 per 1000) have been achieved in recent years. Furthermore, technological development has been impressive.

It should, therefore, not come as a great surprise that not only is it possible to live in Europe’s cities, but also that the average life expectancy is now significantly higher than in other parts of the world. However, the economic situation in Europe is not without its problems. The high cost of living, the high levels of crime, and the high levels of unemployment are all factors that contribute to the problem. In addition, the high levels of immigration have led to a decrease in the birth rate, which has implications for the future of the population. The current economic situation in Europe is also characterized by high levels of debt, which has led to a decrease in the standard of living for many people. However, the European Union has implemented a series of measures to address these problems, such as the introduction of the euro, the creation of the European Central Bank, and the implementation of the European Social Fund. These measures have been successful in reducing the high levels of unemployment and improving the lives of many people. As a result, Europe is now considered to be a model for other parts of the world.

Africa, a forgotten continent

What is it that sets Africa apart? What are the problems of this great continent, where 1 billion people live? Why is Africa the continent with the highest rates of famine, disease, and poverty?

There are many factors, but they are all connected with a poor economic situation.

Sadly, for many years Africa has been the victim of the four enemies of the Apocalypse who have spread their disease: the four winds, war, plague (AIDS), and death. They destroy everything in their wake, leaving behind misery and suffering.

In most Sub-Saharan African countries, around 40% of the population live in poverty, i.e., less than 1 dollar per day. What is even more alarming is that unlike some regions in Asia, this proportion has not improved over the years. What is more surprising is that this is happening in a continent that has 23% of the world’s oil reserves, 40% of its gold and 30% of its platinum, plus it has 60% of the planet’s fertile land.

According to FAO and UNICEF sources, practically one-third of the population of Sub-Saharan Africa suffers from famine [1]. Moreover, the number of people who do not have enough food is increasing every year. In this region, 100,000 people die of hunger every day, among whom 45,000 are children. The causes are the unstoppable population growth, low agricultural productivity, and the fact that most cereal crops (wheat, corn, soybean, rice, etc.) are used to produce biofuels, or are exported to China or India where the demand for food is increasing by year. As the spokesman for the United Nations Jean-Ziegler said, “today’s use and promotion of biofuels is a crime against humanity” (2009).

Naturally, the most immediate consequence of famine is malnutrition: 30 million people in Sub-Saharan Africa suffer from scurvy, which makes them more vulnerable to disease [1, 3].

Moreover, 285 million people in this region (34% of its population) do not have access to safe drinking water, especially rural areas (52%). As a result of drinking dirty water, 4000 children die of diarrhoea daily. To this can be added 45% of the population who do not have proper sanitation. This is a particularly common scenario in the suburbs of large cities [7]. Africa endures huge hardships; in the regions of central Africa do not have any electricity supply. In fact, 50% of the population of Sub-Saharan Africa is without electricity. A large number of rural hospitals are also without power, or only have a supply for 3-4 h per day, while only 7% of the region’s hydroelectric potential is currently being exploited.
Primary prevention of preterm birth

The prevalence of preterm birth has increased, despite efforts to treat pregnant women with symptoms of preterm labor (PTL). In the United States, the preterm delivery (PTD) rate increased from 16.6% in 1990 to 11.7% in 2011, in Germany from 7.3% in 2007 to 9.0% in 2013, and in Portugal from 6.8% in 2004 to 9.6% in 2006. Numerous medical and surgical procedures have been used to treat or prevent spontaneous PTL. There is a need to revisit strategies to reduce the rate of preterm birth.

Definition of prevention

The term “prevention” means “general measures to avoid bad conditions.” The objective of this communication is to present a framework for the prevention of spontaneous PTL leading to PTD. The conventional approach in epidemiology is to divide prevention into primary, secondary, and tertiary levels, and these concepts could be applied to the prevention of PTL. In this case, primary prevention would consist of interventions directed to all women, which are implemented before or during pregnancy, to reduce risk [6]. Secondary prevention measures are directed toward reducing the risk in women with already assessed risk factors (i.e., tocolysis in patients with spontaneous PTL). Tertiary prevention refers to the measures deployed to improve maternal outcome after a PTD has occurred (i.e., administration of surfactant to mitigate respiratory distress syndrome).

Prevention of PTL and PTD

Treatments to reduce the risk of PTL and PTD, such as tocolytic treatment, antenatal corticosteroids, and surgical treatment (cerclage or cervical occlusion), are considered to be secondary or tertiary prevention measures. For primary prevention strategies against PTL and PTD, there is a need to acknowledge and evaluate the risk factors involved. Such primary prevention may uncover benefits that are beyond secondary and tertiary measures. Moreover, through education and public policy, such benefits may depend on sound scientific evidence and may require decades of research effort.

Successive prevention is not a single entity, but a collection of conditions (phenotypes) caused by multiple pathologic processes [18]. Hence, it is unrealistic to assume that a single measure would be universally effective to prevent this condition. Improved understanding of the mechanisms of the disease responsible for such particular phenotype and continued efforts to develop early treatments and interventions would be required to accomplish this goal. At this point, some general ideas can be proposed in discussing primary prevention measures employed to reduce spontaneous PTD.

Iatrogenic risk factors

Reducing the rate of induction of labor and elective cesarean delivery (without labor) is one approach that can be employed to decrease the rate of PTD [22]. However, some PTDs would be required for maternal or fetal indications (e.g., in cases of intrauterine growth restriction or preeclampsia).

Multiple gestations after assisted reproductive technology (ART) procedures can increase the risk for PTL and PTD. This risk remains elevated when conception occurs with ART, even in singleton gestations. Thus far, recommendations aimed at reducing the number of multiple gestations after ART (one embryo transfer) have achieved success in some countries in Europe [2, 7].

Preconceptional primary prevention includes the education of women and health-care providers about the evidence, which states that repeated smears in menstruation (repeated abortion and uterine curettage) is associated with an increased rate of subsequent PTL and PTD [3, 6, 20, 22].
Academy’s Paper

Giovanni Monni*, Maria Angelica Zoppì, Ambra Luculano, Alessandra Piras and Maurizio Arzì

Invasive or non-invasive prenatal genetic diagnosis?

DOI 10.1515/jpm-2014-0055

About 40 years ago, invasive prenatal diagnosis techniques were introduced in obstetrics. Initially, amniocentesis was performed followed by placental biopsy, fetoscopy, fetal blood sampling (FBS), and chorionic villus sampling (CVS). These procedures, while invading the uterine environment, have made it possible to proceed with the retrieval of biological tissue of fetal origin for analysis and definitive diagnosis [6, 20, 21, 27]. The development of such techniques was facilitated by improvements in instrumentation and technology, and was further propelled by the advancement of cytogenetics and molecular genetic techniques [3, 14, 22].

However, invasive prenatal diagnosis carries the inherent risk of fetal loss, which is low, but not negligible (amniocentesis and CVS approximately 0.3%–0.5%, and FBS 1%–2%). In addition, there is a significant economic burden from the costs associated with laboratory techniques. Public health programs of nations interested in the utilization of invasive procedures have generally limited their use to high-risk cases, where the risk of procedure-related loss is comparable to the risk of an affected fetus for a given condition [25, 26]. As a result, in the 1980s amniocentesis was offered to women at higher risk of trisomy 21 based on maternal age alone, if there was an increased risk due to prior complications or pre-existing conditions (i.e., chromosomal aberrations in the parents or in prior offspring), or because of prenatal detection of fetal malformations or other abnormal ultrasound findings. The initial policies led to an offering of invasive prenatal diagnosis to 5% of all pregnant women (positive screen rate), with a 40% detection rate for trisomy 21.

With the advent of biochemical screening tests using maternal serum in the second trimester, the “triple” and “quadruple” screen, the detection rate of trisomy 21 increased to 60% [28]. Meanwhile, with advancements in ultrasound, numerous reports were published that identified sonographic “markers” for trisomy 21, leading to additional screening with a “genetic ultrasound” in the second trimester [1]. However, second trimester ultrasound for the purposes of screening an unselected population never gained universal acceptance, and was primarily used in high-risk populations (i.e., a woman with advanced maternal age that wished to avoid invasive testing). At this time, second trimester amniocentesis was the primary invasive diagnostic test practiced, while fetal blood sampling by cordocentesis was utilized when a diagnostic test was desired later in the second trimester, often in the setting of identification of a fetal anomaly in the second trimester ultrasound. As mean maternal age at childbirth continued to increase, especially in Western countries, alongside increasing scientific advancements, the number of indications for prenatal diagnosis rose. This trend led to an increased rate of invasive prenatal diagnosis, based on maternal age alone up to 15–20% in some nations, and spurred a search for new solutions.

In the mid-1990s, as an important turning point was the use of ultrasound to measure fetal nuchal translucency at 11–14 weeks [17], along with maternal serum biochemical screening, pregnancy associated plasma protein A (PAPP-A), and free beta subunits of human chorionic gonadotropin (free beta-hCG), for the screening of trisomy 21 [24]. With a similar invasive testing rate as maternal age alone at 5%, the combined test led to a detection rate of approximately 90% for trisomy 21 (in the setting of a positive test, the odds of an affected fetus were 1:20). The introduction of the nuchal translucency measurement raised the issue of certification, reproducibility, and reliability of


Academy's Paper

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Fetal mild ventriculomegaly: still a challenging problem

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Ventriculomegaly (VM) is defined as an enlargement of the lateral ventricles of the developing fetal brain. Measurement of the size of the fetal cerebral lateral ventricles is recommended as part of the fetal scan routinely performed during the second trimester to screen for fetal anomalies. The measurement is done at the level of the atria of the lateral ventricles filled by the echogenic choroid plexuses, visible in an axial plane of the fetal brain showing also the frontal horns of the lateral ventricles and the cavum septi pellucidum. The calipers are positioned on the internal margin of the medial and lateral walls of the atria, at the level of the gnomon of the choroid plexus, on an axis perpendicular to the long axis of the lateral ventricle [14]. An atrial width of < 10 mm is considered normal. VM is diagnosed when the width of one or both lateral ventricles, measured according to the criteria described so far, is ≥ 10 mm. Measurements between 10 and 15 mm constitute mild VM, also defined as borderline (Figure 1); values above 15 mm constitute severe VM. Some authors [27] use the term "milder VM" and "mild to moderate VM" to indicate measurements of 10-12 and 12.1-15 mm, respectively. Other authors [4] restrict the term "mild VM" to measurements between 10 and 12 mm. The most commonly used terminology, however, is "mild VM" referring to atrial measurements between 10 and 15 mm and this terminology will be used in the following discussion.

Mild VM can be bilateral or unilateral [15]. Usually in the screening ultrasound examinations, only the lateral ventricle distal to the transducer is measured as the proximal one is obscured by reverberation artifacts. Efforts should be made in order to visualize both ventricles and recognize unilateral and bilateral mild VM (Figure 2).

Mild VM may be associated with a variety of anomalies (brain malformations, genetic syndromes, chromosomal abnormalities, and infections) or can be isolated. The prevalence of isolated mild VM is extremely variable and has been reported ranging from 0.15% to 0.7% [1, 25]. The finding of mild VM represents a cause of anxiety for the parents and a difficult task for the clinician. In order to offer appropriate counseling, an accurate diagnostic work-up is needed. The diagnostic work-up should include the following steps:

- ruling out associated anomalies
- ruling out for congenital infections
- ruling out for feto-necrotic alloimmune thrombocytopenia
- ruling out for chromosomal abnormalities
- monitoring the development of mild VM in the progressing pregnancy.

Once the diagnostic work-up is completed an appropriate counseling can be offered to the parents.

Ruling out for associated anomalies

Mild VM may be associated with neural and extraneural anomalies. The percentage of association ranges from 10% to 71% with an average value of 41.4% [3, 8, 11-13, 17, 18, 23, 25, 29]. With regard to the central nervous system anomalies, an accurate and systematic evaluation of the fetal brain allows the recognition of several both severe and subtle anomalies [5].

Mild VM may also be the first sign of brain anomalies recognizable only in the third trimester or even after delivery, such as cortical malformations. The mean percentage of anomalies not recognized at the time of the first diagnosis of mild VM is 12.8% [3, 11, 13, 15, 18, 20, 27]. A recent review of nine studies reporting data on postnatal imaging, showed a prevalence of previously undiagnosed findings of 12.9% [21]. This better result is probably the consequence of the improvements in the prenatal diagnosis of subtle brain anomalies such as agenesis of the corpus callosum.
Academy’s Paper

Ritsuko K. Pooh*

Sonoembryology by 3D HDlive silhouette ultrasound – what is added by the “see-through fashion”?

DOI: 10.1515/jem-2016-0008

Introduction

Advances of fetal ultrasound technology have established a field of sonoembryology [1, 2] which is still evolving. Recent advances of prenatal ultrasound technology have been remarkable and lead immense acceleration in understanding of human development. No matter how much the molecular genetics progresses and no matter how greatly the sequencing technology improves, the fetal ultrasound is the only technology with direct observation of fetal structure and function from the early gestation age. The anatomy and physiology of embryonic development is a field where medicine exerts greatest impact on early pregnancy at present, and it opens fascinating aspects of embryonic differentiation. Recent development of three-dimensional (3D)/four-dimensional (4D) sonography has revealed structural and functional early human development in utero [3–6]. 3D/4D sonography moved prenatal diagnosis of fetal anomalies from the second to the first trimester of pregnancy [7]. No matter how much the molecular genetics progresses and no matter how greatly the sequencing technology improves, the fetal ultrasound is the only technology with direct observation of fetal structure and function from the early gestation age.

The 3D transducers take several hundreds or thousands of two-dimensional (2D) ultrasound images over a short arc. In other words, 3D image is the accumulation of 2D images. With current clinically available equipment, 3D sonographic reconstruction is fast, with high resolution, giving ultrasound the ability to image in real time. Also, 3D ultrasound allows volume data to be stored and manipulated long after the patient has left the examination room. Storage of a single volume of data is easy and quick, yet the stored volume permits interpretation of the scanned region in multiple planes [8]. 3D/4D ultrasound has improved its functions with high definition live (HDlive) technology and furthermore, great advances of ultrasound technology have produced new applications of HDlive silhouette and HDlive flow.

The further evolution was the exciting applications of HDlive silhouette and HDlive flow imaging technology. This article demonstrates detailed and comprehensive fetal structural images and angiograms of normal and abnormal fetuses in early gestation and the first trimester of pregnancy, depicted by 3D HDlive silhouette and flows, which closely resemble those from anatomical or embryological atlases or scientific documentaries, and describes clinical significance and pitfalls of those novel applications.

HDlive (high definition live) technique

In the history of 3D/4D ultrasound technology, the great achievement was HD (high definition) live technology. This technology is a novel ultrasound technique that improves the 3D/4D images. HDlive ultrasound has resulted in remarkable progress in visualization of early embryos and fetuses and in the development of sonoembryology [9]. HDlive uses an adjustable light source and software that calculates the propagation of light through surface structures in relation to the light direction [10]. The virtual light source produces selective illumination,
Editorial

Shari E. Gelber, Debra Taubel and Frank A. Chervenak*

American medical education: the evolution of excellence

DOI 10.1515/jpm-2013-0048

Despite a formal medical education system that only dates back to the mid-1700s with the founding of the first medical school in the United States (University of Pennsylvania: D’65), the USA is respected for its pursuit of excellence [1]. Excellence in medical education is due to the American cultural system that values the concept of a meritocracy that demands continued evaluation and improvement.

Excellence in clinical care, education, and research is the essence of American medicine. Meritocracy is a fundamental American value that facilitates this goal. Since the time of our nation’s independence in the 18th century, the value of advancement based on success is celebrated in American life and academic institutions. The notion that job security as well as promotion is often based on concrete deliverables (financial stability, academic publications, grant funding) helps drive the academic medical system toward excellence.

A special aspect of the American academic medical center is that of the faculty practice in which physicians perform “private practice” under the auspices of the medical school. The main responsibility of these physicians is clinical care and they may not be directly linked to the research mission of the university [2]. Income generated from patient care supports physicians’ salaries as well as the cost of running the practice. The “taxes” generated by the practice are used to subsidize other missions of the department such as teaching, research, and care for the uninsured. The department pays for rent, professional liability, and support staff, freeing the clinician to focus on patient care and not practice management.

One way American physicians can distinguish themselves is through additional training. As the benefits of working with colleagues with other skill sets has become clear, medical schools are now expanding training to allow for completion of dual degree programs including the MD/PhD, MD/MPH, MD/JD and MD/MBA [3].

Another path to career advancement is through both institutional and geographic mobility. It is accepted and encouraged for physicians to move. Often a move will occur because of an opportunity at another institution. Leadership positions as division directors and department chairs are rarely given to the “next in line” at an institution. Instead, national searches are conducted to ensure getting the “best candidate”. In addition to career advancement for an individual, this mobility encourages the spread of new ideas and technologies. Students, residents, and faculty who may have become complacent with doing things the institutional way are now challenged with new ideas and technologies. This is in contrast to some other countries where the expectation is to stay at a single institution and where promotion through apprenticeship is often the best path to advancement. Furthermore, US medical students are encouraged to perform elective months outside their institution. Many students perform international electives. Students also participate in electives at other hospitals often with the goal of securing a residency position. These opportunities expose students to the way medicine is practiced in different geographic regions and with different patient populations.

The American medical system encourages physicians to achieve independence. Medical training is formalized into highly structured medical school, internship, residency, and fellowship. These educational opportunities are time limited unlike other countries where this is sometimes not the case. After completion of training, there is no expectation of continued apprenticeship, a commonplace occurrence in some other countries. The goals of American training programs are to produce fully functioning independent physicians. Junior aspiring physicians may seek out mentorship for discussion and

• **Kurjak**, First ten years of International Academy of Perinatal Medicine – Which lessons we have learned and what are future challenges. J. Perinat. Med. 2016; 44(7): 733–735

• Ferraz T, **Matias A.** Late pregnancy – a clue to prolonging life? J. Perinat. Med. 2017;45(4):399.401


Neonates of mothers who have had kidney or liver transplantation

Prematurity and low birth weight

According to two meta-analyses published recently by Deshpande et al., the overall live birth rate in the post-transplant kidney and liver population is high, reaching 73.9% and 73.5%, respectively [3]. Nevertheless the complication rate is also high, with preterm delivery observed in about 40% of pregnancies [4]. The prematurity and/or the small-for-gestational age neonate is a vulnerable patient and the long-term consequences of these conditions seem to reach far beyond early childhood. The acute risks of prematurity may include but are not limited to respiratory distress syndrome, necrotizing enterocolitis, invasive infections, and central nervous system injury [5]. It is agreed that the risks are more pronounced in the kidney post-transplant population. The mean birth weight as well as mean gestational age at delivery are in general distinctly lower in kidney recipients, which most probably depends on the underlying condition with higher frequency of arterial hypertension [6]. According to a recently published prospective report concentrating on pregnancy outcomes in the current setting of medical care of the UK post-transplant kidney population, premature birth occurred in 52% of cases, with 48% of infants having low birth weight (<2500 g), and 24% being small for gestational age [7]. Very preterm birth (<32 weeks of gestation) occurred in 9% of cases. The same group also gathered prospective data on neonatal outcomes in UK liver recipients showing that low birth-weight infants occurred in 37% and small for gestation in 21% of cases. None of the liver recipients in this cohort experienced very preterm birth (<32 weeks of gestation) with 42% of infants born before 37 weeks of gestation [8].

Fetal effects of immunosuppressive medications

All the immunosuppressants administered to the mother cross the placenta and are transported by the umbilical vein.
First 10 years of the International Academy of Perinatal Medicine – which lessons we have learned and what are future challenges

Any academy in the world is a society of people of significant intellectual achievements (learned people). They are institutions of individual authority who are trying to advance doctrine, and to produce views on different issues of science and to advice the taken actions in issues related to science.

Academies can and should have a presence in the life of society, without becoming part of politics, but they should provide expert advice when summoned and express competent opinions and reactions to events of global importance.

The IAPM was founded in 2006 on the initiative of presidents of four scientific societies: the World Association of Perinatal Medicine (WAPM), the European Association of Perinatal Medicine (EAPM), and the International Society “The Future of a Patient” (IFAP) and has broadened. The IAPM continues to meet in various capital cities all over the world, holds scientific congresses, and publishes discussions on current topics of perinatal research and patient care from a global point of view.

The aim of the IAPM is to provide a place for study, reflection, dialogue, and for the preservation of perinatal medicine, especially in aspects such as healthcare, the appropriate use of technological advances, and the sociological and humanistic dimensions of the field.

The IAPM should be responsible for research, education, standards. It has the potential of being a leading influence in the world of perinatal medicine.

A prominent advantage of the Academy is the continuous availability of its leaning and acting experts. This is a compensatory potential compared with societies whose relatively frequent change of leading experts is common.

Future challenges

The importance of perinatal medicine is growing rapidly and is making great and varied scientific progress. More and more evidence now indicates that perinatal life is a major determinant of adult health and disease. So for instance the increasing realization that new maternal lifestyle choices now need to be made as well as prenatal care. Even in this domain, for instance in obstetrics, the role of perinatal conditions, such as smoking, alcohol use, and nutrition, has been recognized as important factors in determining adult health and disease. Therefore, the need for international cooperation and the exchange of information about best practices is crucial.

The IAPM plays a key role in fostering international collaboration and promoting the exchange of information and knowledge. It has organized numerous congresses, workshops, and training programs, bringing together experts and stakeholders from different countries and domains.

In conclusion, the IAPM is an essential platform for the advancement of perinatal medicine, providing a valuable resource for the global perinatal community. Its work continues to contribute to the improvement of perinatal care and the well-being of mothers and babies worldwide.
Academy's Paper

Tiago Ferraz* and Alexandra Matias

Late pregnancy – a clue to prolonging life?

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Abstract: The relation between fertility and longevity has always been a subject of study and controversy. Indeed, life expectancy extension is found to be tied to late births. This conclusion can be drawn from social-observational studies like the Long Life Family Study in New England and the New England Centenarian Study on which was found that women whose last birth was after 40 years of age are more likely to live longer. Recently, a group in Israel published a review on animal and human studies that shed some understanding on the cellular mechanisms behind the association between pregnancy and tissue regeneration and repair. These studies shed some understanding to draw biological plausibility on the association between late pregnancy and life expectancy.

Keywords: Anthropology, late pregnancy, regeneration, tissue repair.

Introduction

Prolonging life has always been a hot subject of research in many different areas of medicine.

Regarding the effect (if any) of pregnancy in longevity and tissue regeneration, we may consider the social/demographic studies as well as animal tests.

In fact, the importance of life course on health and mortality differentials in later life is increasingly recognized, both because past experiences exert strong influences on current circumstances and because accumulated stresses may have long-term influences.

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In an England-and-Wales-based social study, Grundy and Tomassini [1] pointed out that parenthood, as a major component of most people’s lives with substantial short- and long-term implications, may exert stresses, role alterations and changes in the allocation of personal and family resources. This may well be associated with physiological and psychological effects of pregnancy and childbirth.

The relationship between parity and lifespan is uncertain, with evidence of both positive and negative relationships being reported previously [2]. From an evolutionary perspective, it has been proposed [2] that a tradeoff exists between increased fertility and decreased human lifespan. Resources are preferentially allocated to fertility and child raising in the early to middle part of life, being diverted from somatic maintenance functions that are required for extended longevity. McArth et al. [3] proposed that parity itself may have no direct relationship to lifespan, but rather high parity could be merely a reflection of men and women who are destined to live longer lives.

Data from the Long Life Family Study [4] also helped in understanding more about the relationship between parity, fertility and lifespan. Three hundred and eleven women who survived past the oldest 5th percentile of survival (according to birth cohort–matched life tables) were identified as cases, along with 151 women who died at ages younger than the top 5th percentile of survival were identified as controls. Looking at the cases of all 462 women, the study found a significant association with older maternal age, whereby women who had their last child after 35 years had twice the odds of survival to the top 5th percentile of survival compared with women who had their last child before 29 years. More specifically, women having their last child between the ages of 35 and 37 years had an odds ratio of 2.08. The odds ratio for older women was 1.92.

Similarly, an analysis of the New England Centenarian Study [5] cohort data revealed that women who gave birth to a child after 40 years of age had four times greater odds of being a centenarian compared with women from the same birth cohort who had their last child at a younger age.

As one may find, the observed association leads to several interesting questions. First, does the association hold under modern conditions? With increasingly late
Academy's Paper

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Antenatal corticosteroids: current controversies

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Introduction

Treatment with antenatal corticosteroids (ACS) has been known for decades and became standard care following the 1994 consensus published by the American National Institute of Health (NIH). The NIH published an amendment in 2000 [1] with three main recommendations, namely (a) women who are expected to deliver within 7 days, between 24+0 and 34+6 weeks' gestation, are considered as candidates for ACS treatment, (b) a single course includes two intramuscular injections of 12 mg betamethasone given 24 h apart or dexamethasone, four doses of 6 mg, 12 h apart; and (c) repetitive doses should be reserved for clinical trials. This standard of care has been endorsed almost unanimously and endured the last 15 years of practice.

The initial indication for ACS was reducing the incidence of neonatal respiratory distress syndrome (RDS) - a clinical approach which was confirmed in a comprehensive Cochrane review by Roberts and Dalziel [2], and was subsequently extended to generally reduce neonatal morbidity and mortality. Regardless of being an integral part of managing preterm labor, ACS treatment presents new controversies that need answers and primary, one may ask how, after so many years of using the standardized protocol, and as will be shown below under ‘Question of timing’, only about half of the patients receive a complete course of treatment. Hundreds of articles were published on issues related to ACS treatment in the last few years and this review updates and discusses some of the newer controversies, the order of which are not related to their importance.

ACS before and after the ‘window of opportunity’

Numerous studies [2] confirmed that ACS treatment reduces infant mortality by 31%, risk of developing RDS by 44%, and the risk of developing intraventricular hemorrhage (IVH) by 66%. In addition, ACSs reduce the risk of developing necrotizing enterocolitis (NEC), the need of respiratory support, incidence of intensive care admissions, and sepsis during the first 84 h of life. Not surprisingly, it was questioned whether these beneficial effects should be restricted to the ‘window of opportunity’, namely after 24 and before 35 weeks’ gestation.

Laboratory studies have shown that corticosteroids accelerate structural as well as functional changes in the fetal lung between 22 and 24 weeks’ gestation (at the canalicular stage) and several cohort studies showed that ACS decreased the mortality and cerebral palsy rates of infants born between 21 and 25 weeks’ gestation [3]. These data led to the idea to extend the lower limit of gestational age for ACS to 23 weeks.

Evidently, cohort studies are not entirely suitable to exclude confounders such as the possibility that women who received ACS very early in pregnancy also received closer follow-up and delivered in a more favorable environment. In addition, the safety of ACS at such gestational ages has not been established yet, especially the potential effect of ACS on fetuses that eventually remain undelivered until a late stage in pregnancy.

In general, ACS are not given beyond 34 completed weeks. However, in light of the increasing incidence of near term birth combined with the higher incidence of respiratory morbidity in infants born by elective cesarean section before 39 weeks’ gestation, it was suggested that ACS might be indicated in pregnancies scheduled for an elective abdominal birth at <39 weeks.

The first study on Antenatal Steroids for Term Elective Caesarean Section (ASTEGS) found in 2006 that ACS in such circumstances deceased by 59% the incidence of transient tachypnea of the newborn (TTN) [4]. A more recent study [5] found that the neonates had less respiratory morbidity after elective cesarean when the mother
Perinatal critical care and ethics in perinatal medicine: the role of the perinatologist

Introduction

Critical care management of life-threatening conditions during pregnancy is an indispensable component of perinatal medicine [1, 2]. Ethics is an essential dimension of perinatal critical care [3]. Like other aspects of critical care medicine, perinatal critical care is an area of clinical practice with considerable potential for ethical conflict. Rather than wait for such conflicts to occur, it is far better for patients, their families and perinatologists to anticipate and seek to prevent ethical conflicts. In this paper, we therefore emphasize a transcultural, transnational and transreligious preventive ethics approach that appreciates the potential for ethical conflicts and adopts ethically justified, clinically applicable strategies to prevent those conflicts from occurring. Preventive ethics helps to build and sustain a strong physician-patient relationship [4], which is especially important in perinatal critical care [1-3]. We first define ethics, medical ethics, and the fundamental ethical principles of medical ethics beneficence and respect for autonomy. Second, we define the ethical concept of the fetus as a patient. Third, we define critical care as a trial of management, with short-term and long-term goals. Fourth, we provide an ethical framework for a preventive ethics approach to perinatal critical care to guide perinatologists in patient care.

Ethics, medical ethics and ethical principles

Ethics has been understood in the global histories of philosophy and theology to be the disciplined study of morality. Morality addresses what our behavior ought to be. Ethics aims to improve morality. Medical ethics is understood as the disciplined study of morality in medicine with the goal of improving medical morality by clearly identifying the obligations of physicians to patients. Medical ethics should not be confused with the many sources of morality that exist globally. These include, but are not limited to, law, the world's religions, ethnic and cultural traditions, families, the traditions and practices of medicine (including medical education and training) and personal experience. Medical ethics since the eighteenth century European and North American national Enlightenments has been secular [1, 3, 5, 6]. It makes no reference to God or revealed tradition, but to what reason discourse requires. At the same time, secular medical ethics is not intrinsically hostile to religious beliefs. Therefore, ethical principles and virtues should be understood to apply to all physicians in all countries, regardless of their personal religious and spiritual beliefs [1, 3, 5, 6]. The resulting professional responsibility models of obstetric ethics [2] and perinatal ethics [3] is transnational, transcultural and transreligious.

The traditions and practices of medicine are based on the professional obligation to protect and promote the health-related interests of the patient. This obligation tells physicians what morality in medicine ought to be, but in very general, abstract terms. Providing a clinically applicable account of that obligation is the central task of medical ethics, using ethical principles [1, 3, 5, 6].

The ethical principle of beneficence in general requires one to act in a way that is expected reliably to produce the greater balance of benefits over harms in the lives of others. To put this principle into clinical practice requires a reliable account of the clinical benefits and harms relevant to the care of the patient, and of how those clinical goods and harms should be reasonably balanced.
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Peripartum cardiomyopathy – from pathogenesis to treatment

Introduction

At the beginning of the 21st century, cardiac diseases remain the main cause of death in pregnant women in many countries. One of the most common cardiovascular diseases associated with pregnancy is peripartum cardiomyopathy (PPCM) [1]. The etiology of this disease is unknown, but factors such as infection, inflammation and autoimmune processes may underlie the pathogenesis of its development [2]. The symptoms of this pathology are typical for a left ventricle (LV) cardiac insufficiency, however, due to the specific physiological condition during pregnancy and peripartum, its first signs may be masked by complaints typical for normal pregnancy [3]. Furthermore, its clinical course may differ, one course being cardiac failure, with abrupt deterioration of the patient's condition and mortality rate reaching up to 28% and another course being normalization of cardiac insufficiency parameters in 23% of the patients after 6 months [3–5].

PPCM is a rare condition, however, it represents a serious risk of death and therefore, it is crucial to have current knowledge of it to enable its differentiation and treatment. In this publication, we present the most recent reports on the etiopathogenesis, diagnosis and treatment of patients with PPCM.

Definition

According to the definition by the European Society of Cardiology from 2011, PPCM is an idiopathic cardiomyopathy occurring at the end of pregnancy or several months after delivery and presenting with cardiac insufficiency secondary to systolic dysfunction of the LV in a previously healthy woman [4, 6]. Its diagnosis is made based on exclusion because other causes of cardiac insufficiency should be excluded before a diagnosis of PPCM is considered [4].

Epidemiology

Although PPCM is a rare condition, complicating 1 in 300 to 1 in 4000 pregnancies, it is associated with a very high mortality rate for mothers, reaching up to 28% after 6 months of therapy [4]. Of those patients who survive, 27%–52% develop cardiac insufficiency (New York Heart Association [NYHA] class III or IV) [7]. Most of the PPCM cases occur after delivery, in 49% of the patients within the 1st month, in 36% of the patients in the 2nd or 3rd month and in 15% of the patients, in the 4th or 5th month [3].

Predisposing factors include parity, diabetes, smoking, arterial hypertension, pre eclampsia, undernourishment, mother’s age (advanced age, teenage pregnancies), the use of tocolytic agents, and anemia in pregnancy [6]. Furthermore, according to the EUH Observational Research Programme, the increased use of assisted reproduction and an increased incidence of multiple pregnancies increases the likelihood of PPCM [8–10].
Academy's Paper

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Pregnancy after malignant disease – challenges and possibilities

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Introduction

The incidence of malignant disease increases with age and reaches its peak after 50 years of age. But, on the other hand, there is a significant number of children and young women in reproductive age who suffer malignancies. In the last few decades, treatment of malignant disease has improved significantly. Thus, there is a significant increase in children, adolescents and young people who reach the first 5 years, with a realistic chance of survival. Around 80% of patients in whom malignant disease is diagnosed before age 15 will survive the first 5 years, and 70% of them will survive 10 years after being diagnosed [1]. Carcinoma occurrence in children has increased in the last decades. But it is encouraging that survival rates have increased as well. In Europe, children's cancer survival rates are higher in Northern countries and lower in Eastern ones. In Great Britain, children's survival rate within 10 years is about 75%. This figure is more than double that of 50 years ago [2]. Unfortunately, in developing countries, this rate is still very low: 10% for a 5-year period [3]. Child malignancies are different from adult ones. The most frequent tumors affecting children are as follows: leukemia (the most frequent, accounting for 30%), brain and spinal cord tumors, Wilms tumor (nephroblastoma), neuroblastoma and lymphoma (both Hodgkin and non Hodgkin). Patients being diagnosed between 15 and 29 years of age account for 86% of all invasive cancers in the United States, which is about 700,000 new cases every year. It is also estimated that over 1,000,000 women of reproductive age have suffered cancer. In Europe, the estimated number is 130,500 annually [4-6]. Longer life expectancy is the main reason for the increased number of young women surviving cancer who are considering motherhood in the future.

With regard to future pregnancies, some questions that should be addressed when facing cancer in children, adolescents and young women are discussed in the following.

How is fertility preserved when treating malignant disease?

When a patient is facing a malignancy, the main objective is healing. But at the same time, the treatment plan should be carefully selected and should take into account the patient’s reproductive future.

Most oncologic treatments imply specific gonadotoxic effects. Chemotherapy with alkylating agents and abdominal pelvic irradiation may produce a reduction in primordial follicles that, in turn, causes temporary or permanent ovarian function loss. This may manifest as acute ovarian insufficiency during treatment, shortly thereafter or later as premature early menopause, even before 40 years of age [7, 8].

The gonadotoxic effect depends on the age of the patient (her ovarian reserve [OR]), the chemotherapeutic agents used and their dosage. If the treatment plan includes pelvic irradiation, this may worsen the patient's reproductive function in the future.

Five groups of alkylating agents are the first line of chemotherapy, although they have the most potent gonadotoxic effect, especially if they are used in combination. Some of such agents are cyclophosphamide, etoposide, melphalan, busulfan and chlorambucil, and these are the agents with a higher risk. Cisplatin and carboplatin, with low cumulative doses, and Adriamycin, with use of intermediate risk. Treatment protocols with bleomycin, actinomycin D, vincristine, methotrexate and fluorouracil, without alkylating agents, are of low risk [9].

The gonads are very sensitive to radiotherapy, and the extent of damage that it may cause depends on the dose and irradiation field. High radiation doses on the hypothalamus and pituitary, as well as total body irradiation,
Academy's Paper

Wanda Guzierska-Majewska, Dorota A. Borka-Opska* and Miroslaw Wielgos

Is pravastatin a milestone in the prevention and treatment of preeclampsia?

Introduction

Preeclampsia (PE) is one of the major disorders of pregnancy and is responsible for one of the main causes of morbidity and mortality in pregnant women. It is a systemic vascular disorder which complicates 5%–6% of pregnancies and increases the risk for severe disorders and death in both, mother and fetus, premature birth.

Abnormal implantation and placental are of key importance for the development of PE. Angiogenic imbalance, i.e., an imbalance between pro-angiogenic factors that are in favor of local inflammation result in generalized vascular endothelial dysfunction leading to increased vascular resistance to placentation.

An angiogenic imbalance seems to be of crucial importance for PE pathophysiology and closely correlates with disease severity and clinical manifestations of PE. It is characterized by the diminished production of vasodilating and angiogenic factors, the upregulation endothelial growth factor (VEGF), plasminogen activator (PAI), and transforming growth factor β (TGF-β) as well as overexpression and release of anti-angiogenic factors such as soluble fms-like tyrosine kinase (sFlt) and vascular endothelial growth factor (VEGF) antagonist and soluble endoglin (sEng) [1–4]. Another theory explaining the pathophysiology of PE claims that PE is linked to the decreased expression of or low placental hormone expression (human/carbon monoxide [HCO]) activity. The HMOX system is responsible for the anti-inflammatory and anti-oxidative mechanisms but it also negatively regulates the angiogenic balance. The impairment of this, endogenous antioxidant system results in endothelial dysfunction and can contribute to the maternal endothelial dysfunction [5]. Abnormal placental growth originating from endothelial dysfunction in turn, leads to the emergence of clinical manifestations, including preeclampsia (Fig. 1).

PE may lead to complications, both maternal and fetal, affecting the mother and the fetus. Early complications observed in pregnant women include swelling, edema, proteinuria, hemodynamic, and obstetric changes. The impact of PE in the course of pregnancy may include placental abnormalities or diagnosed intravascular coagulation. PE may also alter the placenta leading to intracranial growth retardation, chronic and acute hypertension, and long-term consequences of pregnancy, such as fetal death in utero. Children born to mothers with PE are at a higher risk for recurrent preterm pre eclampsia, cardiovascular disease and metabolic disease in adulthood [5,6].

Numerous studies have been conducted for several years on the development of collective methods to prevent PE. The results of a meta-analysis published in 2016 indicate that treatment with aspirin, in pregnant women treated in a small but significant reduction in the risk of maternal complications due to a reduction in placental involvement. However, without reducing the risk, the complication, although not long-term, lasts up to 16 weeks of gestation PI. There is also interest in low molecular weight heparin (LMWH) to prevent placenta-mediated pregnancy complications, including PE. However, the data concerning its efficacy are conflicting.

Highly active advances in the prevention and treatment of PE, in recent years, focused on the discovery of the phenomenon as the only effective method used to prevent various maternal complications. Such an approach, however, is usually associated with numerous advantages and side effects, previously described in the literature.
The first trimester aneuploidy biochemical markers in IVF/ICSI patients have no additional benefit compared to spontaneous conceptions in the prediction of pregnancy complications

Abstract

Objectives: The aim of this study was to determine if the levels of biochemical markers in in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) pregnancies differ from those in spontaneous pregnancies in order to verify if these biochemical markers could predict pregnancy outcome in IVF/ICSI pregnancies.

Methods: This was a prospective observational study performed in a group of 151 patients who underwent a combined first trimester prenatal screening (ultrasound scan and serum markers). All patients were divided into two groups according to the mode of conception: IVF/ICSI pregnancies (study group) and spontaneous conceptions (control group). The concentrations of first trimester biochemical markers were measured as multiples of median (MoM) and were compared between the study and control groups. Analyzed pregnancy complications included: preterm delivery (PTD), small for gestational age (SGA), gestational hypertension (GH), preeclampsia (PE), and gestational diabetes (GDM).

Results: The analysis was performed on 105 IVF/ICSI and 206 spontaneously conceived pregnancies, with complete data regarding outcome. There were no significant differences in the concentrations of biochemical markers between the analyzed groups. First trimester aneuploidy prenatal marker, maternal serum alpha-fetoprotein (MSAFP) levels were lower in IVF/ICSI patients compared to spontaneous patients, although the difference was not significant. SGA was more frequent in IVF/ICSI pregnancies (23.8%) than in spontaneous pregnancies (17.9%). Of the patients with SGA, 29 were delivered prematurely (15.8%).

Conclusions: The trend for lower PAPP-A MoM was not statistically significant in either group, although the results were in agreement with previous studies. The first trimester biochemical markers in modern reproduction techniques (ART) pregnancies do not seem to have additional effect on predicting the risk of pregnancy complications.

Keywords: First trimester biochemical, free PAPP-A, level, MSAFP, pregnancy outcome.

Introduction

The number of children born after assisted reproduction techniques (ART) exceeded 6.1 million according to 2019 estimates, with this proportion of in vitro fertilization (IVF) patients ranging from 0.8% to 4.1% of all deliveries in different countries [1]. In Poland, over 10,000 IVF/intracytoplasmic sperm injection (ICSI) procedures were initiated in 2016 with a 38.5% success rate [2]. Our study was conducted with a sample size of 301 patients, compared to 3000 IVF pregnancies each year seek minimal surveillance [3].

Since the introduction of IVF, various concerns have been raised regarding the poorer perinatal outcome of ART singleton, especially in terms of perinatal delivery (PIN) [1, 3, 4]. However, these cases are not completely clear and need to be understood. First of the concepts is the advanced maternal age. The mean maternal age already implies a greater risk of various complications, but also various pathologies of pregnancy.

For current first trimester gestational screening program markers, the measurement of third trimester (VT) Doppler, additional markers of aneuploidy are now
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