13th Annual Meeting of the Egon and Ann Diczfalusy Foundation

Scientific Programme and Abstract Book

18 – 19 October, 2019, Prague

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Tamás Bitó, Cristian Furau, Rares Gherai, Peter Koliba, Alexandra Vejnovic

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Egon and Ann Diczfalusy Foundation

for

Supporting Research in Reproductive Health

In collaboration with the Medical Faculty, University of Szeged (Hungary), Department of Obstetrics and Gynaecology, University of Szeged, the Reproductive Health-working Group of the Szeged branch of the Hungarian Academy of Sciences, University of Novi Sad (Serbia), Czech Menopause and Andropause Society (Czech Republik) and "Vasile Goldis" Western University of Arad (Romania)

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Dear Colleagues, Dear Guests,

We are happy to organize the 13th Diczfalusy Award Lecture (DAL) symposium in Prague in this Fall. It is a great pleasure to welcome you.

In 2007 Professor Egon Diczfalusy's dream became reality by establishing a Foundation to support research in Reproductive Health and to provide updated knowledge to obstetricians-gynaecologists mainly in Central-Eastern Europe and accelerate the networking with building up research connection besides friendship.

To foster its aims, the Foundation organises a scientific symposium every year. The 13th annual meeting, the DAL 13 is jointly organized with the Czech Menopause and Andropause Society of the Czech Medical Society of J. E. Purkyně. The meeting's venue is the historical city of Prague, the capital of the Czech Republic and it takes place on 18-19 October 2019. On behalf of the Scientific Committee and the Presidium of the Foundation, It is my pleasure and privilege to invite you to participate in this event.

We look forward to the pleasure of welcoming you in Prague and hope that the excellent scientific programme and the internationally outstanding speakers will give you useful scientific merit.

You will experience an unforgettable memory during this event in the friendly atmosphere of the host city and also by tasting the famous Czech beer and discovering the beauty of the capital!

The 13th consecutive meeting clearly proves that Prof. Diczfalusy's dream has come true. I hope the successful cooperation and friendship will keep this vision alive further on.

Yours,

Professor emeritus Dr. György Bártfai

President of the "Egon & Ann Diczfalusy Foundation"

Prof. Dr. Egon Diczfalusy
1920 - 2016

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Gyula TELEGDY (H)

György THALER (H)

Hans-Rudolf TINNEBERG (D)

Aleksandra VEJNOVIC (SRB)

Tihomir VEJNOVIC (SRB)

Frederick WU (UK)

18 October 2019, Friday

10:00 – 12:00 Board Meeting

13:00 – 14:15 Lunch symposium - Special Session

Medical treatment of uterine fibroids – 10 years of experience with Ulipristal Acetate.

Chair: György Bártfai

13.00 – 13.30 Hans-Rudolf Tinneberg (D)

Long-term medical treatment of uterine fibroids

13.30 – 14.00 Robert Hudeček (CZ)

Uterine fibroids and reproductive disorders. Surgery or pharmacological treatment?

14.00 – 14.15 Q&A session

14:15 – 14:20 Opening addresses – Presidium

14:20 – 14:40 Keynote lecture 1.

Chair: Giuseppe Benagiano (I)

14:20 – 14:40 Gian Carlo Di Renzo (I)

Environmental chemicals & climate and human reproduction.

14:40 – 15:00 Key note lecture 2.

Chair: Peter Koliba (CZ)

14:40 – 15:00 Jean-Michel Foidart (B)

Estetrol/Drospirenone as a Combination Oral Contraceptive and the Results of the Phase 3 studies

15:00 – 15:45 Bestowal Ceremony

15:00 – 15:05 Young Scientist Award

Laudation by Cristian Furau (RO)

15:05 – 15:20 Acceptance speech: Dan Dumitrascu-Biris (UK)

Handover of the Medal by Tihomir Vejnovic (SRB)

15:20 – 15:25 Life-time Scientific Achievement Award

Laudation by György Bártfai (H)

15:25 – 15:45 Acceptance speech: Frederick Wu (UK)

Handover of the Statue by *Gyula Telegdy (H).*

15:45 – 16:00 Coffee Break

16:00 – 18:15 Session 1.

Chair: Gábor Németh (H) and Tihomir Vejnović (SRB)

16:00 – 16:20 Giuseppe Benagiano (I)

Reducing caesarean section rates in Europe

16:20 – 16:40 Béla Szabó (RO)

Diagnosis and prevention of prematurity

16:40 – 17:00 Izhak Blickstein (IL)

The contribution of twins conceived by assisted reproduction technology to the very preterm birth rate

17:00 – 17:20 Dieter Bettelheim (A)

Management of placenta accreta and increta after delivery

17:20 – 17:40 Aleksandar Stefanović (SRB)

Cancer and pregnancy

17:40 - 18:00 Katarina Jeremic (SRB)

Pregnancies after conservative treatment of early stages of endometrial cancer – our experiences

18:00 – 18:20 Discussion

19 October 2019, Saturday

9:00 – 9:20 Keynote lecture 3.

Chair: György Bártfai (H)

9:00 – 9:20 Sir Sabaratnam Arulkumaran (UK)

Professionalism and personal experience.

9:20 – 10:50 Session 2. Young Diczfalusy Fellows Session

Chair: Ludwig Kiesel (D), Cristian Furau (RO),

Aleksandra Vejnović (SRB)

9:20 – 9:35 Peter Koliba jr. (CZ)

Deep endometriosis of bowel

9:35 – 9:50 Richard Nagy (H)

On the origin of common trisomies

9:50 – 10:05 Anca Panaitescu (RO)

Fetal defects in maternal autoimmune disorders

10:05 – 10:20 Dan Dumitrascu-Biris (UK)

Prediction and prevention of preeclamspia

10:20 – 10:35 Isidora Dickov (SRB)

Analysis of the series of cases of placenta accreta at the Clinic for Gynecology and Obstetrics of the Clinical Center of Vojvodina

10:35 – 10:50 Discussion

10:50 –11:10 Coffee Break

11:10 – 13:30 Session 3

Chair: János Annus (H), Petru Chitulea (RO)

11:10 – 11:30 Dan Apter (FL)

Drospirenone a progestin only oral contraceptive: Efficacy, Safety and Unscheduled Bleeding.

11:30– 11:50 Peter Koliba (CZ)

Chronic pelvic pain in women

11:50 - 12:10 Ludwig Kiesel (D)

Novel targets in endometriosis.

12:10 – 12:30 Zuzana Niznaska (SK)

Puberty to menopause – reproductive transitions

12:30 -12:50 Discussion

12:50 –13:10 Valedictory lecture

Chair: György Thaler (H)

12:50 – 13:10 Herjan J.T. Coelingh Bennink (NL)

Estrogens, estetrol and breast cancer

13:10 – 13:45 Best Posters session

Chair: Gheorge Furau (RO), Zuzana Nižňanská (SK), Britt-Marie Landgren (S)

Presentation of the best 3 posters.

13:45 – 14:00 Closing Remarks

Giuseppe Benagiano (I)

Peter Koliba (CZ)

György Bártfai (H)

Young Scientist Prize

The Prize is given annually to an internationally acknowledged young investigator, for his/her achievements in improving Reproductive Health.

One side depicts a mother with her child and Professor Diczfalusy's Life-Motto: **Empathy, Science and Hope**

The other side shows the Dom square with the Votive Church and the Microbiological Institute of the University, Szeged and a frequently quoted phrase from him: **Medicina, Anchora, Salutis**.

The previous years' awarded were:

For The Young Scientist Award

- 2007 Dr. Nathalia Maria Cruz (Sweden)
- 2008 Dr. Eszter Ducza (Hungary)
- 2009 Dr. Claudio Avram (Romania)
- 2010 Signe Altmae, Ph.D. (Sweden)
- 2011 Dr. Cristian Furau (Romania)
- 2011 Dr. Dunja Lonchar (Serbia)
- 2012 Dr. Attila Molvarec (Hungary)
- 2013 Dr. Silvia Visentin (Italy)
- 2014 Dr. Salvatore Gizzo (Italy)
- 2015 Dr. Gyula Richárd Nagy (Hungary)
- 2016 Dr. Nicolea Bacalbasa (Romania)
- 2017 Dr. Aleksandra Vejnovic (Serbia)
- 2018 Dr. Michael Feichtinger (Austria)

The Diczfalusy Prize

The prize acknowledges one's lifetime scientific achievements in the field of research on Reproductive Health with a miniature version of the original statue of Klara Tobias, called the „Hungarian Pieta 1956".

For The Lifetime Scientific Achievement Award

- 2007 Prof. Salvatore Mancuso (Italy)
- 2008 Prof. Britt-Marie Landgren (Sweden)
- 2009 Prof. Mahmud Fathalla (Egypt)
- 2010 Prof. David Archer (USA)
- 2011 Prof. Biran Affandi (Indonesia)
- 2012 Prof. Badri Saxena (India)
- 2013 Prof. Mark Bygdeman (Sweden)
- 2014 Prof. Ilpo Huhtaniemi (Finland)
- 2015 Prof. Gyula Telegdy (HU)
- 2016 Prof. Giuseppe Benagiano (Italy)
- 2016. Erik Bogsch (Hungary)
- 2017 Prof. Marius Craina (Romania)
- 2018 -

13th Annual Meeting of the
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Laudations and Abstracts of Lectures

(in order of appearance)

Special Session

Medical treatment of uterine fibroids – 10 years of experience with Ulipristal Acetate.

Long-term medical treatment of uterine fibroids

Hans-Rudolf Tinneberg (D)

Frauenklinik Nordwest Krankenhaus, Frankfurt, Germany

Uterine fibroids are common, benign gynecologic tumors with a significant negative impact on women's lives and affecting one in three to four women in reproductive age. Surgery may not be a suitable option for all patients, therefore a long-term medical treatment of fibroids is important. There are limited treatment options available for women with moderate to severe symptoms of uterine fibroids who wish to avoid operation.

Clinical studies demonstrate that ulipristal acetate 5 mg is an effective treatment for long-term intermittent management of symptomatic uterine fibroids and providing a fast symptoms control. This review summarizes efficacy and tolerability data relevant to the intermittent use of ulipristal acetate highlight the medical treatment importance.

The clinical experiences with Ulipristal acetate 5 mg have confirmed this option is an effective and generally well tolerated treatment for patients and the only approved long-term alternative in women with symptomatic uterine fibroids for whom surgery is not an option.

The review includes the conclusion of the Article 20 Pharmacovigilance which considers that the benefit-risk balance of the ulipristal acetate 5mg containing drug remains favourable subject to the agreed amendments to the product information and risk minimization measures.

Uterine fibroids and reproductive disorders. Surgery or pharmacological treatment?

Robert Hudeček (CZ)

Department of Gynecology and Obstetrics, Faculty of Medicine, Masaryk University and University Hospital Brno, Czech Republik

The review paper deals with international innovative approaches in the treatment of uterine myomatosis in relation to reproductive dysfunctions.

The dominant issue is uterine myomatosis as an epidemiological effect of reproductive dysfunction factor. Presentation with innovative procedures within clinical diagnostics and classification, morphology and histology of fibroids and the influence of fibroids on the results of assisted reproduction.

Chapter on pharmacological possibilities of therapy of myomatosis of color rays of long-term personal experience of the author in the field of international cooperation in solving multicentric tax assessments. The result of this research activity is the author's contribution to

the registration of a revolutionary pharmacist of the group Selective Progesterone Receptor Modulators for the Treatment of Fibroids in Clinical Practice.

Surgical treatment of myomatosis is presented by a set of papers analyzing perioperative procedures and their results using pharmacological support agents prior to use during myomectomy. Minimization of peroperative haemorrhage complications, active prevention of adhesion formation after myomectomy and in connection with intrauterine adhesions in relation to perspective independent areas - reproductive surgery. Presented results of the author's work are supported by stakeholders of scientific research projects, grants, research plans and international clinical studies.

Keynote lecture 1.

Environmental chemicals & climate and human reproduction.

Gian Carlo Di Renzo, MD, PhD, FACOG, FRCOG, FICOG

Dept of Obstetrics and Gynecology & Centre of Perinatal and Reproductive Medicine, University of Perugia, Perugia, Italy

"ENVIRONMENT" Includes Industrial chemicals Agricultural chemicals Physical agents (heat, radiation) By-products of combustion and industrial processes (dioxin) but also Foods and nutrients , Prescription drugs teratogens Lifestyle choices and substance abuse , Social and economic factors.

Our global health report card shows in the last decades a marked increase in non-communicable diseases (NCDs) such as obesity and diabetes, neurodevelopmental disorders, reproductive compromise, respiratory and thyroid dysfunction, cancers. At the same time there was a marked increase in unregulated global chemical production, use and disposal, and now we have increasing evidence that environmental chemicals (e.g., endocrine disrupting chemicals) and air pollution contribute to NCDs and developmental origins of health and disease (DOHaD).

Some diseases increased in incidence over the past 40 years but our genes have not changed over that time. Moreover there were reported recent "epidemics" of diabetes, asthma, attention deficit hyperactive disorders (ADHD), obesity due to environmental, dietary and behavioral changes. It is clear nowadays that we will never understand the etiology of diseases without an understanding of the role of "environment".

Exposure to toxic environmental chemicals is linked to millions of deaths and costs billions of dollars every year Examples: seven million people die each year because of exposure to indoor and outdoor air pollution; pesticide poisonings of farmworkers in sub-Saharan Africa is estimated to cost $66 billion between 2005-2020; health care and other costs from exposure to endocrine disrupting chemicals in Europe are estimated to be at a minimum of 157 billion Euros a year; and, the cost of childhood diseases related to environmental toxins and pollutants in air, food, water, soil and in homes and neighborhoods was calculated to be $76.6 billion in 2008 only in the United States. (Di Renzo et al, 2015)

We are drowning our world in untested and unsafe chemicals and the price we are paying in terms of our reproductive health is of serious concern. Reproductive health professionals witness first hand the increasing numbers of health problems facing their patients, and preventing exposure to toxic chemicals can reduce the burden on women, children and families around the world. Every person in the world has measurable contaminants in their body. Mixtures of chemicals are the rule. Contaminants are found also in pregnant women: environmental tobacco smoke, lead, perfluorinated compounds, perchlorate, mercury, pthalates, bisphenol A…."To a disturbing extent, babies are born pre-polluted….". Every pregnant woman in the U.S. has at least 43 toxic exogenous chemicals in her body . Virtually all pregnant women have measured levels of lead, mercury, toluene, perchlorate, bisphenol A (BPA). Studies have documented that each of these chemicals can be harmful to human reproduction and/or development. We have forgotten rapidly the story of Diethylstilbestrol in the 1950's, Methyl mercury in the 1960's…and the Endocrine Disruptors of the twenty-first century. EDCs = endocrine disrupting chemicals, are chemicals or mixtures of chemicals that interfere with any aspect of hormone action at any time of development and/or during the life course and produce adverse developmental, reproductive, neurological, and immune effects in both humans and wildlife. Empirical data have shown that neonatal medical exposure can be 3 orders of magnitude or more above exposures in the general population. One phthalate, Di (2-ethylhexyl) phthalate (DEHP), is an endocrine disruptor and can cause cancer, may affect human reproduction and development, is related to increase in preterm birth, crosses the placenta, found in breast milk. It has been found also higher serum levels of several phthalates in girls with premature thelarche. Reproductive toxicants alter follicles, steroids and function and pathologic changes in the testes and decreased sperm numbers are consistent effects across studies.

FIGO has created n ad hoc Committee to address all these issues and has released a seminal paper on FIGO opinion on reproductive health impacts of exposure to toxic environmental chemicals (Di Renzo et al IJGO 2015) , suggesting the following actions:

Recommendation 1: Advocate for policies to prevent exposure to toxic environmental chemicals;

Recommendation 2: Work to ensure a healthy food system for all;

Recommendation 3: Make environmental health part of health care;

Recommendation 4: Champion environmental justice.

Support the "Precautionary Principle" that in the absence of evidence that a chemical is safe, precaution should prevail even if there is no evidence of cause and effect. A chemical should never be released if a concern exists about its safety. Health care providers should face no risk for evaluating patients, providing care, and providing advice. The onus of SHOWING HARM MUST SHIFT from the public to the chemical industry. We must have preemption addressed directly: Just as in medical liability reform we have NOT wanted to undermine the advances states have made legislatively, it is incumbent upon us to maintain the advances in environmental stewardship and health that leaders have set in the individual states and countries.

Key note lecture 2.

Estetrol/Drospirenone as a Combination Oral Contraceptive and the Results of the Phase 3 studies

Jean-Michel Foidart (B)

No abstract arrived

Bestowal Ceremony
Young Scientist Award

Curriculum Vitae

PERSONAL DETAILS

Full Name:	**Dr. Dan Andrei Dumitrascu-Biris**
Address:	83 Lollard Street, SE116 PX, London
E-mail Addresses:	andreidandumi@yahoo.com, dr.dan.biris@gmail.com

Education and training :

2016	present	Clinical Fellow Maternal-Fetal Medicine	King's College Hospital	Sub - specialty Maternal Fetal Medicine
2013	2016	Clinical Fellow Fetal Medicine	King'S College Hospital, Fetal Medicine Center, University College London	Sub-specialty Fetal Medicine
2009	2013	Specialty training in Ireland and Romania	BEGA Women's Hospital and Mullingar Regional Hospital	Specialty doctor

Working experience:

From	To	Name and location (city) of University	Subject or specialty	Level of course (diploma, degree, certificate, etc)
April 2014	Present	King's College Hospital	Maternal Fetal - Medicine	Senior Registrar post CCT

Details of Courses and Conferences attended over the last 5 years:

Year	Name of course	Details
2018	ROBUST course	King's College Hospital
2018	K2 CTG training program	King's College Hospital
2017	ROBUST course	King's College Hospital
2016	St. George's CTG Course	St George's Hospital
2014	Advanced Fetal Cardiology course	St. Thomas Hospital Evelina

PUBLICATIONS:

1. Severe hypertension, preeclampsia and small for gestational age in women with chronic hypertension diagnosed before and during pregnancy – Nzelu D., Dumitrascu-Biris D., Kay P., Kametas N., Nicolaides K., Pregnancy Hypertension, Oct 2018
2. Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, preeclampsia, and small for gestational age - Nzelu D., Dumitrascu-Biris D., Kametas N., Nicolaides K., Pregnancy, AJOG March 2018
3. Fetal fraction in maternal plasma cell-free DNA in the prediction of spontaneous preterm delivery – Quesada M., Francisco C., Dumitrascu-Biris D., Nicolaides K., Poon L., Ultrasound in Obstetrics and Gynaecology, 2014
4. The IONA® test for first-trimester detection of trisomy 21, 18 and 13.' Ultrasound in Obstetrics and Gynecology. Poon CYL, Dumidrascu-Biris D, Carla Francisco, Fantasia I, Nicolaides, KH 2015.
5. Pregnancy outcomes in women with previous gestational hypertension – A cohort study to guide counselling and management Diane Nzelu, Dan Dumitrascu-Biris, Katharine Hunt, Cordina Mark, Nikos Kametas

Laudation of Dr Dan Andrei Dumitrascu-Biris

Dan Andrei Dumitrascu Biris is a Romanian doctor born on 23.03.1981. He is currently working as a Senior Registrar in Maternal Fetal Medicine at *King's College Hospital*, London. He graduated University of Medicine and Pharmacy "Victor Babes" Timisoara. In his first years of residency he worked both in Romania and Republic of Ireland.

Since 2013 he started working with Professor Kypros Nicolaides, in London, at King's College Hospital, where he specialized in Maternal Fetal Medicine.After nearly two and a half years of training in this field he graduated with Diploma in Fetal Medicine, award given by Fetal Medicine Foundation. He specialized in fetal therapy, pregnancy scanning (first to third trimester) and management of complicated pregnancies, maternal medicine and other fetal procedures.
After this Fellowship he joined the obstetric team at King's College Hospital where he continued to work in both clinical and non clinical area. He joined the Maternal Medicine team looking after pregnancies complicated by hypertension, diabetes, renal disease and other medical problems. After more then 10 years working mostly in UK, he is a senior consultant for ultrasound in obstetrics and gynecology, natural deliveries, cesarean section, open benign gynecological surgery, laparoscopic surgery, TOP, obstetrical and gynecological small surgery, hysteroscopy, etc. In the last 5 years he has attended and was a trainer for OB-GYN courses developed by King's College Hospital London, St. George's Hospital London, St. Thomas Hospital Evelina, Royal College of Obstetricians and Gynecologists, Cork University Hospital, Mullingar Regional Hospital, UMF Timisoara.

He has continued the academic work commenced with Professor Nicolaides and has managed to publish more then 10 articles in well known journals such as Ultrasound in Obstetrics and Gynaecology, KH, International Journal of Women's Cardiovascular Health, Journal of Human Hypertension, AJOG. Also he was invited and had numerous presentations in major international conferences being an important FMF figure such as: London (UK), Allicante, Mallorca (Spain), Athens, Crete (Greece), Amsterdam (Netherlands), Nice (France), Timisoara (Romania), Ljubliana (Slovenia) and has won the poster first prize at the National Conference of Minimal Invazive Surgery (Oradea, Romania, 2008).

He plays mentoring role, supervising and teaching junior colleagues, nurses and medical students who were allocated to him by his supervising consultant. He was responsible for the Journal Club Meetings and once a month to present the Morbidity and Mortality Meetings at King's College Hospital of London.

Added to his professional and research activity, I can confirm key skills such as: proven ability to work effectively and as part of a team, proven creativity and flexibility in case of new challenge, Diplomacy, self control, good manager, communication and inter-personal skills having an excellent feedback from his patients, junior colleagues, consultants and midwives, ability to work in a multicultural environment. He speaks very good English, French and Romanian, but also has good knowledge of Serbian language.

I recommend him for the Young Diczfalusy Award 2019.

MD Furau Cristian George, PhD

Lecturer, Head of the Pathophysiology Discipline at the Western University „Vasile Goldis" of Arad

Acceptance speech

Chronic hypertension in pregnancy: outomes

Dan Dumitrascu-Biris

King's College Hospital, London, United Kingdom

Objectives: To assess perinatal outcomes in women with chronic hypertension (CH) stratified into four groups according to their blood pressure (BP) control in the first trimester.

Study Design: Prospective cohort study of women with CH and singleton pregnancies booking at <14 weeks gestation. Groups 1-3 had pre-pregnancy CH; Group 1 had BP<140/90mmHg without antihypertensives (N=234), Group 2 had BP<140/90mmHg with antihypertensives (N=272) and Group 3 had BP>140/90mmHg despite antihypertensives (N=194). Group 4 included women without history of CH, presenting with BP>140/90mmHg (N=100).

Outcomes Measures: Periventricular leukomalacia, chronic lung disease, retinopathy of prematurity, necrotising enterocolitis, hypotension), delivery before 37 weeks, caesarean section, fetal growth restriction (FGR), admission to the neonatal (NNU) and intensive care unit (ICU), ventilation, total parenteral nutrition (TPN), respiratory distress syndrome (RDS), sepsis, hypoglycaemia and jaundice.

Results: Perinatal mortality and abruption complicated 1.5% and composite outcome 2.5% of cases, while 20.5% of babies needed admission to the NNU (ICU 6.9%).

Conclusion: The high rates of adverse perinatal outcomes in women with CH are worse in those who do not normalise their BP in the first trimester.

Bestowal Ceremony
Life-time Scientific Achievement Award

Frederick Chung Wei Wu's short scientific CV

Position

Professor Emeritus of Medicine and Endocrinology, Centre for Endocrinology and Diabetes, Institute of Human Development, Faculty of Medical and Human Sciences, University of Manchester

Qualifications

B.Sc. Hons (First Class) (Edin)	1970
M.B., Ch.B. (Edin)	1972
M.R.C.P. (U.K.)	1975
M.D. (Edin)	1983
F.R.C.P. (Edin)	1989
F.R.C.P. (Lond)	1995

Positions and Employment

- 2003 – 2018 Professor of Medicine and Endocrinology, Department of Medicine, University of Manchester, Honorary Consultant Physician, Department of Endocrinology, Manchester Royal Infirmary, Manchester, U.K.
- 1994 – 2003 Senior Lecturer in Medicine (Endocrinology), Department of Medicine, University of Manchester, Honorary Consultant Physician, Department of Endocrinology, Manchester Royal Infirmary, Manchester.
- 1992 – 1994 Senior Lecturer, Head of Section of Endocrinology, Department of Medicine, University of Manchester School of Medicine, Honorary Consultant Physician, Hope Hospital, Salford, Greater Manchester.
- 1983 – 1992 Clinical Scientist, Medical Research Council Reproductive Biology Unit, Edinburgh, Honorary Consultant Physician, Royal Infirmary, Western General Hospital and Royal Hospital for Sick Children, Edinburgh.

- 1982 - 1983 Visiting Research Fellow (Professor D.M. de Kretser, O.A, Department of Anatomy, Monash University and Reproductive Medicine Clinic, Prince Henry's Hospital, Melbourne, Australia.
- 1979 – 1982 Senior Registrar in Medicine, Endocrinology and Diabetes, Royal Infirmary and Western General Hospital, Edinburgh (Dr. R.F. Robertson C.B.E., Dr. A.D. Toft C.B.E. & Professor Sir Christopher Edwards)
- 1977 – 1979 Medical Research Council Clinical Training Fellow (Professor D.T. Baird C.B.E.), Department of Obstetrics and Gynaecology, University of Edinburgh
- 1974 – 1977 Registrar in General Medicine and Endocrinology, Royal Infirmary, Edinburgh
- 1973 – 1974 Senior House Officer in General Medicine, Royal Infirmary, Edinburgh
- 1973 – 1973 House Physician to Professor J.A. Strong C.B.E., Western General Hospital, Edinburgh
- 1972 – 1973 House Surgeon to Professor Sir Patrick Forrest, Royal Infirmary, Edinburgh

Honours

- Lifetime Scientific Award of the Diczfalusy Foundation, Hungary, 2019
- The Distinguished Achievement Medal awarded to the Researcher of the Year 2013 in the Faculty of Medical and Human Sciences, University of Manchester).
- Northern Communities Health Foundation Visiting Professorship, University of Adelaide, Australia 2013
- Freemasons Roskill Foundation International Lecturer, lecture tour of four Universities in New Zealand, 2011
- Britain's Top Doctors (Endocrinology) - The Times Newspaper, November 2010
- Claude D. Pepper Older Americans Independence Center, Visiting Professor Lecture, Boston University Medical Center, Boston, USA, 2010
- Egon Diczfalusy Lecture Medal, Karolinska Institute, Stockholm, Sweden, 1996
- Medical Research Council Clinical Training Fellow with Professor D.T. Baird C.B.E., Department of Obstetrics and Gynaecology, University of Edinburgh - Aug 1977 - July 1979
- President, European Academy of Andrology, 2006 - 2010
- Chairman of Examination Committee for the Diploma for Clinical Andrology, European Academy of Andrology, 1997 –2006.
- Treasurer, International Society of Andrology, 1994 - 2001
- Member of the Executive Council, European Academy of Andrology, 1997 to 2013.
- Treasurer, International Society of Andrology, 1994 - 1997 and 1997 - 2001 (second term).
- Chairman, North West Endocrine Society, United Kingdom, 1995 - 1996.

Other Experience and Professional Memberships

- Editorial board member (*present* and past) – *Journal of Clinical Endocrinology & Metabolism, Asian Journal of Andrology, Basic & Clinical Andrology, Journal of Andrology,* Journal of Sexual Medicine, Clinical Endocrinology, Journal of Endocrinological Investigations
- Member of the Annual Meeting Steering Committee, Endocrine Society, 2010 – 2013

- President, European Academy of Andrology, 2006 – 2010

- Chairman of Examination Committee for the Diploma for Clinical Andrology, European Academy of Andrology, 1997 – 2006
- Member of Executive Council, European Academy of Andrology, 1997 - 2006
- Treasurer, International Society of Andrology, 1994 – 2001
- Member of the Steering Committee, Task Force on the Regulation of Male Fertility, World Health Organisation Special Programme of Research, Development and Research Teaching in Human Reproduction., 1992 – 2013
- Founding Member and member of Executive Council of the International Society for the Study of the Ageing Male, 1997 – 2016
- Member of the Clinical Committee, Society for Endocrinology, 1997 – 1999
- Programme committees (1 as chairman) - 5 international scientific congresses
- Advisor (ad hoc) to the World Anti-Doping Agency (WADA) on anabolic steroid abuse
- *The Princeton III* consultation - Cardio-metabolic Risks and Sexual Health – Miami, Fl, USA, 2010
- Since 2003, successfully supervised 2 MD, 12 PhD and 3 MSc theses
- Advisory boards/consultancies for 12 international pharma companies

Research Funding (recent and current)

- Since taking up posts in Manchester, research grant funding totalling £18 million (sole and joint) from MRC, BBSRC, Wellcome, EC and WHO
- European Commission Framework Programme V – European Male Ageing Study: Prevalence, incidence and geographical distribution of symptoms of ageing in men and their endocrine, genetic and psychosocial correlated. €6,100,000 over 7.5 years. January 2002 to February 2010
- Bayer Schering AG - Effects of testosterone on muscle function, physical performance, body composition and quality of life in frail elderly men. £659,390 over 3 years - with J Oldham and M Connolly. September 2004 to July 2009
- BBSRC-LINK Applied Genomics Programme Grant and Astra-Zeneca and GSK - The human serum metabolome in health and disease, with D Kell, G Goodacre, JK Cruickshank, N Purandare, A Burns, G Jayson. £3.9 million over 4 years - January 2005 to December 2009
- World Health Organisation – Sperm suppression and contraceptive protection provided by norethisterone-enanthate plus testosterone undecanoate in normal men US $572,729 over 3.5 years - March 2008 to August 2012
- Medical Research Council - National Survey in Sexual attitude and Lifestyle (NATSAL) 2010 with A Johnson, CH Mercer, K Wellings, W Macdowall, A Copas, P Sonnenberg, C Ison, £5.4 million for five years - August 2008 to July 2013
- Wellcome Trust - National Survey in Sexual attitude and Lifestyle (NATSAL) 2010 with A Johnson, C Mercer, K Wellings, W Macdowall, A Copas, P Sonnenberg, C Ison, B Erens, S McManus and H Wardle £2 million over five years - August 2008 to July 2013
- Bayer Schering AG and the New England Research Institute, Watertown, MA, USA with R Rosen – A registry of Hypogonadism in men. US$ 640,000 over 4 years Jan 2009 – Dec 2013

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4. **Wu FC**, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, O'Neill TW, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Kula K, Lean ME, Pendleton N, Punab M, Boonen S, Vanderschueren D, Labrie F, Huhtaniemi IT; EMAS Group. Identification of late-onset Hypogonadism in middle-aged and elderly men. **New England Journal of Medicine,** 2010; 363: 123-135
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6. **Wu FC**, Tajar A, Pye SR, Silman AJ, Finn JD, O'Neill TW, Bartfai G, Casanueva F, Forti G, Giwercman A, Huhtaniemi IT, Kula K, Punab M, Boonen S, Vanderschueren D; European Male Aging Study Group. Hypothalamic-pituitary-testicular axis disruptions in older men are differentially linked to age and modifiable risk factors: the European Male Aging Study. **Journal of Clinical Endocrinology and Metabolism**, 2008;93:2737-45
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Laudation by György Bártfai (H)

It is a great honour for me to introduce Professor Frederick Wu. I feel personally privileged and delighted to deliver his laudation for getting the Lifetime Scientific Award of the Egon and Ann Diczfalusy Foundation.

He was born in 1942 in Hong Kong. After finishing his college he moved to England for continuing his studies in Kingswood School of Bath and University of Edinburgh, Scotland where he graduated in medicine in 1970.

He reached many appointments in the UK, and he was a Senior Lecturer and Consultant Physician in his mother country, China (Hong Kong) as well. He had achieved many remarkable scientific recognitions in his fields of interest, namely in endocrinology and andrology.
His first appointments were at the University of Edinburgh where he did clinical and research work trough two decades. Afterwards his scientific career continued at the University of Manchester until his retirement.
As far as teaching is concerned: he held regular undergraduate and postgraduate courses at the University of Manchester. He was also a visiting professor in many places worldwide like Melbourne and Adelaide, Australia, Auckland, Wellington, New Zealand or in Boston, USA.
Other teaching activities:
He gives lectures regularly outside Manchester in the UK and abroad in postgraduate training courses organised by national and international societies, including but not limited to the following: International Society of Andrology, World Health Organisation, US Endocrine Society, Australian Socierty of Endocrinology, European Academy of Andrology, European Federation of Endocrine Societies, European Society for Human Reproduction and Embryology, Swiss Endocrine Society.
He has had many acknowledgements, awards and important positions in scientific societies.
Treasurer, International Society of Andrology, 1994 - 2001
Treasurer, International Society of Andrology, 1994 - 1997 and 1997 - 2001
He received the Egon Diczfalusy Lecture Medal, in Karolinska Institute, Stockholm, Sweden, in 1996. At the ceremony, Prof. Diczfalusy was present.
Member of the Executive Council, European Academy of Andrology, 1997 to 2013.
Chairman of Examination Committee for the Diploma for Clinical Andrology, European Academy of Andrology, 1997 –2006.
President, European Academy of Andrology, 2006 - 2010
He was chosen to the top doctors of Britain on the field of endocrinology by the Times Newspaper in November 2010.
Northern Communities Health Foundation Visiting Professorship, University of Adelaide, Australia 2013

He was given the The Distinguished Achievement Medal awarded to the Researcher of the Year 2013 in the Faculty of Medical and Human Sciences, University of Manchester (being nominated for his seminal research into the endocrinology of ageing, successfully co-ordinating the multi-national and multi-disciplinary European Male Ageing Study (EMAS) over the past 10 years and being at the forefront of investigating the importance of testosterone in elderly men). This was our huge common project while scientifically cooperating with a friend made things much easier.
He applied for numerous successful projects and grants.
Since taking up posts in Manchester, research grant funding totalling £18 million (sole and joint) from MRC, BBSRC, Wellcome, EC and WHO
The three most important projects were:

1. European Commission Framework Programme V – European Male Ageing Study: Prevalence, incidence and geographical distribution of symptoms of ageing in men and their endocrine, genetic and psychosocial correlated. €6,100,000 over 7.5 years. January 2002 to February 2010
2. World Health Organisation – Sperm suppression and contraceptive protection provided by norethisterone-enanthate plus testosterone undecanoate in normal men US $572,729 over 3.5 years - March 2008 to August 2012
3. Medical Research Council - National Survey in Sexual attitude and Lifestyle (NATSAL) 2010 with A Johnson, CH Mercer, K Wellings, W Macdowall, A Copas, P Sonnenberg, C Ison, £5.4 million for five years - August 2008 to July 2013

He published a huge number of articles: Selected Peer-reviewed Publications from over 350 in prominent journals like: J Clin Endocrinol Metab and New England Journal of Medicine.

This rich scientific biography can convince everyone that the Foundation made the right decision when it awarded Professor Frederick Wu the Lifetime Scientific Award - a miniature statue symbolizing freedom, selected by the founder, Professor Diczfalusy.

Prof. emeritus Dr. György Bártfai

Acceptance speech

Functional changes in the Hypothalamic-Pituitary-Testicular (HPT) axis in ageing men – longitudinal data from the European Male Ageing Study (EMAS)

Frederick C.W. Wu

Professor Emeritus of Medicine and Endocrinology, Andrology Research Unit, Division of Endocrinology, Diabetes & Gastroenterology, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, United Kingdom.

Ageing is associated with multi-level alterations in the hypothalamic-pituitary-testicular (HPT) axis function affecting both the steroidogenic and gametogenic compartments. It is not clear how this aligns with the clinical scenario of symptomatic older men presenting with low or low normal testosterone (T). Whether the clinico-pathological constructs of hypogonadism,

long established in young patients, can be translated to underpin the management of the burgeoning number of middle aged and older men being referred for possible androgen deficiency, is also uncertain.

I will present prospective follow-up data in the observational cohort of >3000 men from the European Male Ageing Study (EMAS), which describe the natural history of two divergent tracks of HPT axis dysfunctional that underlie the age-related decline in T, based on the physiological classification of hypogonadotrophic (secondary) or hypergondodotrophic (primary) 'hypogonadism'.

The main findings are:- the vast majority of men in the general population men do not become hypogonadal during ageing. Obesity is associated with the development of sexual symptoms with chronic but reversible hypothalamic/pituitary suppression (equivalent to secondary 'hypogonadism') independent of age, usually affecting middle-aged rather than elderly men. In contrast, the less common equivalent of primary 'hypogonadism' found mainly in men over 70 yr of age show a more severe phenotype with sexual and physical symptoms, insulin resistance and co-morbidity compatible with either androgen deficiency or general health deterioration. It is also relatively common to encounter elevated LH with normal testosterone in ageing men - this can be considered to be a state of compensatory 'eugonadism' since they do not have definite features of androgen deficiency, but amongst them will be a small minority who eventually transitions to primary 'hypogonadism'.

Our epidemiological study cannot clearly differentiate between the co-linear symptoms of androgen deficiency and the non-specific features of ageing-related disability or prove causality of clinical features resulting from low T. Nevertheless, our observational data are consistent with results from recent RCTs of T replacement in symptomatic older men with low T. Improved understanding of the aetiology, natural history and potential clinical significance of the age-related changes in the HPT axis can inform designs of future interventional trials and current clinical practice.

Reducing caesarean section rates in Europe

Giuseppe Benagiano

Faculty of Medicine and Dentistry, Sapienza, University of Rome, Rome, Italy

For thousands of years, cesarean section (CS) was carried out on a dying woman to save the life of the baby and mortality for the mother was virtually 100%. Then, in 1876, Edoardo Porro, Professor of Obstetrics and Gynecology at the University of Milan, in an attempt to prevent life-threatening hemorrhage and infection, introduced a technique consisting of uterine corpus amputation and suturing of the cervical stump into the abdominal wall incision. Within five years of his initial operation, he performed 50 cases with a maternal mortality of 58% and an infant survival of 86%, a major advance for the time.

Today, CS are not only performed routinely; in some countries their rate grew exponentially up to almost 50% of all deliveries.

The fundamental question then is: How did cesarean sections, in some 150 years, go from a desperate attempt at saving at least the baby, to an operation performed in up to 50% all of pregnant women, often without a real medical indication? In reality, it would be wrong to believe that an excessive recourse to CS is a new problem. Back in the thirties, John Martin Munro Kerr, Professor of Obstetrics and Gynecology at Edinburgh University, wrote: "*I fear that today more than ever before, there is a danger of abdominal delivery being regarded as the legitimate method of dealing with each and very obstetrical abnormality*" (1).

Today, and not only in Europe, there is a tendency to believe that elective CSs are safer for the mother and the child. The reality though is somewhat different: A systematic search of databases for published studies in human subjects up to 25 May 2017, including: randomized-controlled trials and large (>1,000 participants) prospective cohort studies with ≥1-year follow-up, comparing outcomes of women delivering by CS and by vaginal delivery (VD), found that CS deliveries are associated with a reduced rate of urinary incontinence and pelvic organ prolapse, and an increased risk for subfertility, future pregnancy, and long-term childhood outcomes (2).

Given the trend to an increased use of CSs, it is important to know the attitude of women towards delivering today. Five years ago, a population-based survey of 1000 Italian women found that 80% of them preferred VD if they could freely choose, with a higher preference among older (84.7%), more educated (87.6%), multiparous women (82.3%) and women without any previous CS (94.2%). The main reasons for preferring a VD were: Not wanting to be separated from the baby during the first hours of life, a shorter hospital stay, a faster postpartum recovery. The main reasons for preferring a CS were: fear of pain, convenience to schedule the delivery, perception that a CS is less traumatic for the baby (3).

In the debate over CS there are reasons why the procedure is so popular, first and foremost, the fact that it is safe and simple: New techniques minimize the invasiveness and consequences of the surgical procedure, shortened surgery and hospital stay.

Today three main issues remain controversial: Should women be allowed to choose the mode of delivering their baby independently of a medical indication? Is it sufficient to carry out a CS with just informed consent? If so, what does informed consent really mean? As an

example, women should know that a CS without medical indication is associated with an increased risk of childhood asthma and that exclusive breastfeeding in infancy may attenuate this risk (4).
This means that there is a need for caution in view of well-known specific health risks for infants born by CS. These include: Neonatal depression due to general anesthesia; fetal injury during hysterotomy and/or delivery; increased likelihood of respiratory distress even at term; breastfeeding complications. In addition, concurrent with the trend of increasing CS, there has been an epidemic of both autoimmune diseases (such as type 1 diabetes, Crohn's disease, multiple sclerosis) and allergic diseases (such as asthma, allergic rhinitis, and atopic dermatitis) (5).
A fundamental issue is represented by the importance given to "*The natural way*": Over hundreds of thousand years of human evolution, mother nature found ways to reward the fetus for the danger and the stress of being pushed through the birth canal, by providing it with specific advantages. One in particular has been recently identified and studied: The "*Maternal vaginal microbiota*". The human fetus lives in a germ-free intrauterine environment and enters the outside world containing microorganisms from several sources, resulting in gut colonization. Full-term, vaginally born infants are completely colonized with a diverse array of bacterial families and species (>1000) by the first year of life. Colonizing bacteria communication with the gut epithelium and underlying lymphoid tissues ('bacterial–epithelial crosstalk') results in a functional immune phenotype and no expression of disease (immune homeostasis) (6). When delivered by caesarian section, the very first microbes colonizing the child are derived from contact with the hospital environment and the mother´s skin. The diversity of the human microbiome – the community of micro-organisms that literally share our body space – is in fact set in early life and it has been suggested that the composition of the gut bacterial community might affect the maturation of the infant immune system (7). Indeed, different microbial colonization patterns are associated with VD vs. CS with a consequent diverse early gut microbiota colonization; in turn, this influences the maturation of the infant immune system and health during the first 1000 days of life. This means that the mode of delivery and full breast-feeding both play a major role in ensuring an appropriate development of gut immunity. This has created a new paradigm, whereby gut microbiome influences immunological, endocrine, and neural pathways and plays an important role in infant development.
Infant microbial colonization patterns have the potential to impact physical and neurocognitive development and life course disease risk. Understanding these influences will, not only improve new-born care and parental education, but also guide us on the most appropriate mode of delivery (8).

In conclusion, high rates of CS will continue to be the most likely scenario in Europe and in a number of other countries. Obstetricians and women are both involved in causing these increased rates. Therefore, there is a need for unbiased, evidence-based information to guide both of them in order to optimize the use of CS.
The World Health Organization is playing an important role in this area by: engaging in producing and disseminating accurate information on risks and benefits for both modes of deliveries, including possible long-term risks that at present can only be hypothesized.

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Diagnosis and prevention of prematurity

Béla Szabó

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Introduction: Worldwide, 15 million babies are born too soon every year, causing 1.1 million deaths. The majority (two thirds) of preterm births (PTB) are spontaneous and recurrence risks are high.

Unfortunately, we have no enough criteria to the true clear identification of women at true risk for preterm birth. Identification of risk factors early in pregnancy is an essential component of clinical obstetric care, since early interventions may be effective in reducing the risk of PB.

Material and methods: We performed a review of the recent literature regarding the most important risk factors for premature birth, the main symptoms on the basis of which real premature birth can be predicted and the most important methods of preventing preterm birth.

Results: Risk factors: a history of obstetrical problems, unfavorable socioeconomic status, unhealthful lifestyle, multiple pregnancy are the most common.

The most common method to identify PTB risk is the ultrasonography. The main sign is the cervical length assessment. Other tools include cervical consistence, uterocervical angle, cervical dilatation.

The most common biochemical markers: fetal fibronectin, Insulin-like growth factor-binding protein-1, placental alpha microglobulin-1, phosphorylated insulin-like growth factor-binding protein-1.f Unfortunately, the positive predictive value for PTB, and the specificity of these markers are low, why they are a restricted utility.

In prevention of prematurity smoking cessation, BMI index reduction, cervical length ultrasound screening, progesterone supplementation seems to be effectives.

Conclusion: Currently, there are no efficient methods for the prediction of PTB. Ranking the severity of risk factors is important to identify the true cases of PMB. Currently the measurement of cervical length by transvaginal ultrasound is the only cost-effective method, who could be combined with a biochemical marker to reduce the unnecessary hospitalization costs.

The contribution of twins conceived by assisted reproduction technology to the very preterm birth rate

Isaac Blickstein

Dept. of Obstetrics & Gynecology, Kaplan Medical Center and The Hadassah-Hebrew University School of Medicine, Jerusalem, Israel

Multiple pregnancies are still an adverse outcome of assisted reproduction (ART) whenever more than a single embryo is transferred. As a consequence, the very preterm birth rate is expected to increase in the population.
In this retrospective population-based study we stratified by plurality and gestational age (<32 weeks vs >32 week) all deliveries >24 weeks in women who conceived by ART. We counted the frequencies of all ART liveborn twins among all liveborn infants and among all liveborn twins and frequencies in the subgroup of very preterm births. During the period 1987-2010, there were 13,293 twins (2.73%, range 1.93-3.62%, a nearly 2-fold increase from 1987 to 2010), 6939 infants born after ART (1.42%, range 0.03-2.62%, an 87-fold increase from 1987 to 2010), including 2317 (33.4%, range 14.28-44.83%, a 3-fold increase from 1987 to 2010) twins (0.47% of all deliveries). A total of 425 twin infants (0.99%, range: 1.07-1.2%, insignificant increase) were born at <32 weeks' gestation, including 261 after ART (61.4%, range 20-100%, 5-fold increase).

With these numbers in mind, a single embryo transfer should be considered at all possibilities.

Management of placenta accreta and increta after delivery

Dieter Bettelheim

Division of Obstetrics and feto-maternal Medicine, Vienna General Hospital, Medical University of Vienna

Abnormal placental implantation occurs when placental trophoblasts invade into the superficial uterine endometrium (placenta accreta), into the myometrium (placenta increta), or beyond the uterine serosa (placenta percreta).This lecture deals with the incidence, diagnosis and therapy of this complication which seems to be more frequent in present time. It is of utmost and, in the truest sense of the word, vital importance to be aware of these situations in advance (importance of targeted ultrasound screening).The association between placenta previa accreta and prior cesarean section seems to be obvious because the incidence of placenta accreta increases as the number of previous cesarean sections increases. Patients with an antepartum diagnosis of placenta previa, who have had a previous cesarean section should be considered at high risk for developing placenta accreta. In the event of placenta accreta, the third stage of labor is often prolonged and may be complicated by severe uterine hemorrhage, requiring extensive life-saving surgical interventions such as hysterectomy and manipulation of major pelvic vessels. Massive blood and blood product transfusions are often the norm, and maternal morbidity is reported to be high.

This is the reason why a targeted ultrasound screening should be performed for all women after 2 previous caesarean sections and/or placenta previa. Prenatal diagnosis of placenta percreta is feasible with high sensitivity and specificity for an experienced sonographer using colour doppler sonography. I will talk about the incidence, predisposing factors, diagnosis, clinical implications and management options of this condition by presenting an overview of our management of pregnancy and delivery in these complicated situations.

Cancer and pregnancy

Aleksandar Stefanović (SRB)

Clinic for Obstetrics and Gynecology, Clinical Center of Serbia, Medical Faculty, University of Belgrade

Nowadays we registered much more cases of cancer between young women. Therefore it is strong conetcted with their pregnancies. We know that more then 31% of patients with cervical cancer are up to 40 years old. So there is a need for less radical surgery in patients who are not finished their reproduction. The concept of fertility-preserving surgery in early cervical cancer is radical trachelectomy for stage IA2 or IB disease,. Trachelectomy is a conservative oncologic operation with aim to preserve fertility in early stages of cervical cancer female patients that have realized reproduction. Excised structures in trachelectomy are: cervix, upper 1/3 of vagina, parametria and paracolpia, with preservation of uterine corpus. After removing the vaginal fornix and cervix , uterovaginal anastomosis with non resorptive suture is performed. Indications for trachelectomy are, patients up to 45 years of age who wich to conserve fertility with negative lymph nodes, no distant metastatic disease , FIGO stage cervical cancer staged IA1, IA2, IB1 (tumour size ≤ 2cm with negative lymph nodes), with adequate cervical length, no evidence of expansion of malignat proces on the upper part of the cervical cannal ,squamocellular carcinoma, rarely cervical adenocarcinoma, negative lymph nodes intraoperatively, no metastatic disease, clear resected margins. There is an ongoing debate regarding the need for uterine vessels preservation. Some authors have proved that the preservation of the uterine artery is associated with more favorable restoration of the reproductive function. Others claim that preservation of the uterine vasculature is not necessary for fertility as obstetrical outcomes are similar to those of the historical vaginal radical trachelectomy cohorts. Simple trachelectomy as alternative to radical trachelectomy in selected cases (parametrial involvement rate < 1% in patients with IB1 ≤ 2cm, negative lymph nodes and stromal invasion ≤ 10mm).

Pregnancies after conservative treatment of early stages of endometrial cancer – our experiences

Katarina Jeremic (SRB)

Clinic for Obstetrics and Gynecology, Clinical Center of Serbia, Medical Faculty, University of Belgrade

Diagnosis of a gynecologic malignancy in a young patients often results in sterility as also in reducing quality of life after the treatment. In order to avoid radical standard therapy, whenever it is possible, we offer a patient less radical approach in early stage of gynecological malignant disease. Endometrial cancer is the most common cancer of the female genital tract and female patient less than 40 years may account for 3-14% of all endometrial cancers. The promising fact is that in women < 45yrs the tumor is mostly low risk disease confined to the endometrium whith excellent oncologic outcomes (5 - DFS 99,2%). An increasing number of women are choosing to delay childbearing until later in life so the importance of improving quality of life and preserving fertility is our task force. The European Society of Gynecologic Oncology (ESGO) but also European Society for Human Reproduction as also American Society for Human Reproduction has task force in preserving fertility without compromising oncological oucome.

Conservative management of endometrial cancer is non standard gynecological procedure with no standard clinical recommandations about the therapy but with strict selection criteria for conservative approach. Fertility sparing treatment should be interdisciplinary, with obligate patients counseling and close follow-up schedule and patients will to accept the risks associated with deviation from the standard of care. Conservative approaches of early-stage endometrial carcinoma includes hormonal therapy,in selected group of young patients with endometrial carcinoma age less than 45 years and wishes to preserve fertility, that shows low grade 1 endometrioid adenocarcinomas limited to the endometrium with MRI excluded myomaterial invasion, without evidence of limphovascular space involvement or extrauterine disease (cervical, ovarian ,lymphnodal or any other extra-uterine disease). The diagnosis is proven by two experienced gynoncology pathologists review of analized endometrial samples. It could be collected by biopsy, hysteroscopy or dilatation & curatage and if it possible PgR analysis should not done.

Contemporary consensus standardizing conservative management does not appear either as the optimal agent, dosing, and duration of treatment. Surveillance modalities and frequency after treatment are not standardized. Repeating endometrial biopsies by hysteroscopy every 3 months has been recommended, until there is a complete response or achieving pregnancy. Surgery is recommended if there is no response after 6 months of medicational treatment

The two most common regimens are progestins/medroxyprogesterone acetate (MPA) at 500–600 mg daily and megestrol acetate (MA) at 160 mg daily. An alternative to systemic progestins is the LNG-IUD. A novel hybrid approach that combines local hysteroscopic excision of the tumor with hormone treatment was recently introduced. Series of patients with stage IA EC underwent conservative resectoscopic treatment using a three-step technique first reported in 2005. First, the tumor was removed; second, the endometrium adjacent to the tumor was removed; and, third, the myometrium underlying the tumor was resected.

Fertility after treatment is not guaranteed, even there had been recorded reduced fertility of those treated, and there is a significant need ART (18-60%). Pregancy rate varies up to 33% The higher live birth rates associated with ART. By ART we shortened time to achieve pregnancy until possible relaps. Oncological risk for synchronous endometroides carcinoma ovary in 5 up to 20%, even in macroscopic normal ovaries, the risk of occult ovarian tumour is about 1%. The risk of recurrence remains a reality even for those with complete initial response in 25-40%. Despite highly durable complete response rates of 50%–75%, up to 80% need surgical treatment, so definitive treatment after completion of childbearing is recommended. Future direction should be to conduct larger studies for hysteroscopic EC excision followed by progestin treatment are needed, as also future prospective trials with progestins, LNG-IUD. But also to find out molecular profile of tumor that would be treatened.

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Keynote lecture 3.

Professionalism – reflection in clinical practice

Sir Sabaratnam Arulkumaran

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Professionalism reflects to the concept of a Profession and the characteristics commonly associated with the Professional person. As a doctor there are minimum expectations of us by the patients. These characteristics together forms the foundation of doctor-patient relationship of TRUST & RESPECT. We should have a particular set of skills in our chosen field at a level to be considered as an expert. These skills are acquired through learning, knowledge, training and practice of the relevant skills. Knowledge, skills, communication, and attitude should be demonstrated by qualifications/ accreditation and praise worthy practice. The expertise should be maintained by ongoing learning/CPD & appraisal i.e. Revalidation. As professionals we are expected to have the ability and dedication to achieve certain standards in our work that is acceptable by our peers. We should work and behave in a manner that is appropriate to the nature of our profession i.e. gain respectability; In medicine this includes good standards of personal appearance, appropriate communication and personal conduct i.e. attributes that should confirm to a patient as of acceptable standards. We should do what is right when expected by the law and this should be based on ethical and moral compass and should be a matter of personal pride. Professionalism should include honoring commitments and keeping promises as key aspects of responsibility and reliability. We should ensure that tasks and duties are completed and addressed by taking the initiative and leading by example; because lack of immediate attention to one's duties can be the difference between life and death. Probity is a corner stone of a Professional i.e. Good, Honest, Upright personality, Fair, law abiding and of general good character. Central trust is placed in a medical professional and we should uphold this reputation by our actions. Our actions should be seen as being appropriate and proper by the public and fellow professionals. Professionals should respect the authority and the rule of law and maintain that when managing/ employing others. We should be courteous and should respect the rights, dignity and autonomy of others. We should take pride in doing a job well by paying attention to detail and by taking personal responsibility for our actions and the consequences. As professionals we need to develop and improve our skills and not be satisfied with substandard results – we should seek to put things right. We should acknowledge mistakes, learn from them and take appropriate steps to prevent recurrence.

We should show respect for those who consult us in a professional capacity. We can capture the essential virtues of Professionalism with seven Cs; Commitment, Concern, Communication, Compassion, Command respect by knowledge, skills and behavior, Call for team work and Continued Care. Examples to demonstrate Professionalism will be discussed by reflecting on illustrative cases.

Deep endometriosis of bowel

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Deep endometriosis is defined by infiltrating tissue 5 mm beneath the peritoneal surface. It can cause a complete distortion of the pelvic anatomy and it mainly involves uterosacral ligaments, bladder, rectovaginal septum, rectum and rectosigmoid colon. Although endometriosis is benign disease and the number of women affected by deep endometriosis involving bowel is not so high (5,3-12% of patients with endometriosis), symptoms can be severe and debilitating. Hormonal treatment in this type of affection is usually not effective. Surgical treatment is the method of choice. Depending on the extent of bowel infiltration, surgical treatment can range from bowel (rectal) shaving, discoid resection to segmental resection of affected intestine followed by end-to-end anastomosis. Affection of low rectum, greater extent of the disease, and higher radicality of surgery is associated with higher risk of complications and consequent side effects, such as low anterior resection syndrome (LARS), might occur. In our study we performed 32 laparoscopic segmental bowel (rectum or sigmoid) resections with end-to-end anastomosis between years 2017 and 2018. Surgical treatment had significant positive effect on symptoms (pain relief) and improved quality of life of treated women after 6 months postoperative follow up. The number of complications was consistent with other studies.

On the origin of common trisomies

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Objective: According to the Oocyte Mosaicism Selection model, maternal ovarian trisomy 21 mosaicism might be the primary causative factor for fetal Down syndrome. We hypothesized that this theory could be extended to trisomy 13 as well.

Design & Methods: We collected fetal ovarian tissue samples from seven female fetuses between 16-23 weeks of gestation, after pregnancy termination for non-genetic reasons. All procedures were performed with informed consent and ethical approval from the local ethical committee. We used touch preparation techniques from fetal ovarian tissues: the cut surface of the fetal ovaries was dabbed onto a microscope slide to distribute a thin layer of cells for microscopic examination. To differentiate between germ cells, ovarian stromal cells, and the cells entering their first meiotic prophase, we used an anti stromal antigen 3 immunofluorescence antibody against the meiosis-specific stromal antigen 3 protein. Fluorescence in situ hybridization (FISH) analysis was done on the same slide to determine chromosome 13 numbers in each cell. To evaluate the amount of trisomy 13 in stromal antigen 3 negative and stromal antigen 3 positive cells, we compared immunofluorescence and FISH reaction results.

Results: We were able to detect a proportion of trisomy 13 cells in all cases. The average occurrence of trisomy 13 cells was 0.91 % in the stromal antigen 3 negative cells and 2.04 % in stromal antigen 3 positive cells. The number of the trisomic cells were significantly increased with gestational age (for stromal antigen 3 negative cells $r=0.85$, $p=0.0071$, for stromal antigen 3 positive cells $r=0.93$, $p=0.0038$).

Conclusion: This study indicates that the Oocyte Mosaicism Selection model might be extended to trisomy 13 as well, next to trisomy 21. The crucial factor for trisomy 13 seems to be the pre-meiotic/mitotic trisomy 13 mosaicism, leading to a so-called secondary meiotic nondisjunction of those oocytes having three copies of chromosome 13. We can hypothesize that this pre-meiotic/mitotic nondisjunction happening in the fetal life of the future mother might be the origin of the common trisomies of her fetus.

Fetal defects in maternal autoimmune disorders

Anca Panaitescu

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Maternal autoimmune disorders are characterised by the presence of abnormal autoantibodies. During pregnanancy, these autoantibodies can cross the placenta and act on the fetus, sometimes causing fetal damage. This presentation summarises the development and management of fetal thyroid goitre in response to maternal Graves' disease and / or its treatment with antithyroid drugs, fetal heart block due to maternal anti-Ro and anti-La antibodies, fetal athrogryposis multiplex congenita in association with maternal myasthenia gravis and fetal brain hemorrhage due to maternal autoimmune thrombocytopenia.

Prediction and prevention of preeclamspia

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Objectives: To examine the performance of screening for early, preterm and term pre-eclampsia (PE) at 11-13 weeks' gestation by maternal factors and combinations of mean arterial pressure (MAP), uterine artery (UtA) pulsatility index (PI), serum placental growth factor (PlGF) and serum pregnancy-associated plasma protein-A (PAPP-A).

Study Design: The data for this study were derived from three previously reported prospective non-intervention screening studies at 11 + 0 to 13 + 6 weeks' gestation in a combined total of 61 174 singleton pregnancies, including 1770 (2.9%) that developed PE.

Outcomes Measures: preeclampsia, serum markers

Results: Combined screening by maternal factors, UtA-PI, MAP and PlGF predicted 90% of early PE, 75% of preterm PE and 41% of term PE, at a screen-positive rate of 10%; inclusion of PAPP-A did not improve the performance of screening.

Conclusion: Screening by maternal factors and biomarkers at 11-13 weeks' gestation can identify a high proportion of pregnancies that develop early and preterm PE.

Analysis of the series of cases of placenta accreta at the Clinic for Gynecology and Obstetrics of the Clinical Center of Vojvodina

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Introduction: placenta accreta (PAS) represents placental invasion into the uterine wall deeper than endometrium. It is one of the most serious complications in obstetrics leading to high maternal and neonatal morbidity. Peripartum hysterectomy is often life-saving solution.
Aim: to determine PAS prevalence, risk factors and perinatal outcome in patients with histologically verified placenta accreta.
Material and methods: retrospective study of medical hystories of 29 patients with histologically verified placenta accreta after peripartum hysterectomy operated in the Clinic of Gynecology and Obstetrics of Clinical Center of Vojvodina from January 2007- December 2018.
Results: from January 2007- December 2018 there were 77.218 total deliveries, 22.966 cesarean sections, 64 peripartum hysterectomies, 29 PAS. PAS prevalence increased 4 times. Most PAS patients (62%) were older than 35 years. PAS occured most frequently in third pregnancy, in patients with at least 2 uterine scars and when the time distance from the previous cesarean section was 2 years. The performance of prenatal diagnostics improved during the examined period. There was 70% cases with placenta praevia, and 30% with anterior placenta. Placenta increta constituted 73% of histological findings. Cesarean section was performed at 34+4 GW on average.

Conclusion: prevalence of PAS is increasing. Risk factors for PAS are multiparity, uterine scar, advanced age of the patient and shorter period from the last cesarean section. It is necessary to form a multidisciplinary PAS team, in order to improve the health care of this category of patients.

Keywords: placenta accreta; placenta praevia; peripartum hysterectomy; cesarean section.

Drospirenone, a progestin only oral contraceptive: efficacy, safety and unscheduled bleeding

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Contrary to combined oral contraceptives, progestin only pills do not increase the risk of VTE. Traditional POPs have poor cycle control and stringent pill rules, such as a 3-to-12-hour time window for taking the next pill. Delays occur frequently, reducing contraceptive reliability. A new POP formulation has been developed, drospirenone 4.0 mg with 24 active tablets followed by 4 placebo tablets, designed to try to reduce unscheduled bleeding.

Drospirenone 4.0 mg POP has now been extensively studied. Initially effective ovarian suppression was demonstrated in 64 healthy women aged 18-35. Despite the 4-day treatment-free period, inhibition of ovulation was as effective as that with 0.075mg desogestrel-only pill. In a follow-up study of 121 healthy women, with adding multiple intentional delays of 24 hours in tablet intake, inhibition of ovulation was maintained.

In a prospective, multicenter, non-comparative study in healthy women aged 18-45 years from 41 European sites, Pearl Index was 0.51 (n=713). Drospirenone 4.0 mg also demonstrated a good safety profile and favorable cycle control, thereby providing an important option for a much broader group of women than those for whom previous POPs were recommended.

In a pivotal, multicenter, randomized comparison of drospirenone 4.0 mg to desogestrel 0.075 mg over 9 cycles in nearly 1,200 healthy women aged 18-45, the safety and efficacy findings were confirmed giving a pooled Pearl Index of 0.73. The bleeding profile for drospirenone 4.0 mg was better compared to desogestrel, potentially leading to better tolerability and acceptance. In the drospirenone group, 3.3% discontinued due to bleeding problems, compared to 6.6 in the desogestrel group.

Finally, drospirenone 4.0 mg has been investigated in 111 adolescents aged 12-17 years in a multicenter, open-label trial for six 28-day treatment cycles and an optional 7 cycle extension. Only 12.7% (13 subjects) prematurely terminated the trial during the Core Phase. Incidence of both scheduled and unscheduled bleeding and spotting decreased. Only five subjects (4.9%) prematurely terminated the trial due to irregular bleeding. The number of subjects reporting dysmenorrhea decreased from 46.1% prior to screening, to 29.8% at Cycle 6 and to 17.0% at Cycle 13. At the endpoint, 82.4% rated the tolerability of drospirenone as “excellent” or “good”.

Drospirenone 4.0 mg has been well tolerated, safe and acceptable. The findings distinguish this new-generation estrogen-free pill from traditional POPs by allowing the same flexibility in intake as COCPs, while maintaining contraceptive reliability.

Chronic pelvic pain in women

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Chronic pelvic pain in women is defined as persistent, noncyclic pain perceived to be in structures related to the pelvis and lasting more than six months. Studies using various definitions estimated that its prevalence ranges from 2.1% to 24% of the female population worldwide.

Often no specific etiology can be identified, and it can be conceptualized as a chronic regional pain syndrome or functional somatic pain syndrome. It is typically associated with other functional somatic pain syndromes (e.g., irritable bowel syndrome, nonspecific chronic fatigue syndrome) and mental health disorders (e.g., posttraumatic stress disorder, depression). Diagnosis is based on findings from the history and physical examination. Pelvic ultrasonography is indicated to rule out anatomic abnormalities. Referral for diagnostic evaluation by laparoscopy is usually indicated in severe cases. Curative treatment is very often elusive, and evidence-based therapies are limited. Patient engagement in a biopsychosocial approach is recommended, with treatment of any identifiable disease process such as endometriosis, interstitial cystitis/painful bladder syndrome, and comorbid depression. Potentially beneficial medications include nonsteroidal anti-inflammatory drugs, and analgesics. Pelvic floor physical therapy may be helpful.

Surgical treatment is resorted to after unsuccessful conservative therapy or when there is a high probability that the pain is surgically solvable. Chronic pelvic pain is an indication for laparoscopic evaluation. Karnath and Breitkopf report the occurrence: no pathologic abnormalities were detected in 35% of cases, endometriosis was found in 33%, and adhesions were found in 24%. In select cases, neuromodulation of sacral nerves may be appropriate. Hysterectomy may be considered as a last resort if pain seems to be of uterine origin, although significant improvement occurs in only about one-half of cases. Curative treatment is elusive, and evidence-based therapies are limited.
Comprehensive guidelines for the diagnosis and treatment of chronic pelvic pain have been developed by the European Association of Urology. They include a description of the current understanding of pathophysiology and psychosocial aspects, as well as classification, diagnosis, and treatment.

Chronic pelvic pain is poorly understood and, consequently, poorly managed. This condition is best managed using a multidisciplinary approach. However, in many cases it's not possible to identify a single cause for chronic pelvic pain. In that case, the goal of treatment is to reduce your pain and other symptoms and improve the quality of life.

Novel targets endometriosis.

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Objective: Medical therapy of endometriosis ranges from analgesics to hormonal drugs in order to relieve symptoms either alone or in addition to surgical treatment of endometrial implants, nodules or endometriosis. Almost 2/3 of women treated still suffer from some persisting pain and current therapy appears to have limited long term effect. Therefore novel druggable targets are needed in order to improve the management of endometriosis. In addition, hormonal and non-hormonal targets and associated drugs are required to individualize therapy for affected women.

Design & Methods: A detailed PUBMED research has been conducted in order to analyse existing data on current biological classes in trials as well as new hormonal and non-hormonal drugs. Promising preclinical findings of our lab and others on novel cellular targets will be put into perspective with their potential for future clinical application.

Results: The majority of evaluated drugs in studies target the hypothalamic-pituitary-gonadal axis and estrogen action, indicating that today hormonal therapy is yet in the foreground of endometriosis therapy. The preference of individual drugs seems to differ greatly among different countries. In hormonal therapy the one promising new class appears to be GnRH antagonists. Next to hormonal therapy novel targets arise i.e. drugs aiming at pro-inflammatory mediators and pathways. Endometrial stem cells or dysregulated microRNAs are currently a matter of translational research and show promise as non-hormonal targets for future therapy.

Conclusion: Only a small fraction of completed trials on endometriosis has been published. The main problem for successful novel agents in the treatment of endometriosis is still the lack of detailed knowledge of the mechanisms involved in the pathogenesis, clinical course and recurrence of endometriosis.

Puberty to menopause – reproductive transitions

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There are two main periods in womens life leading to and from the period of reproductive age. These are puberty and manopause. There are disscussions on association between them. There are studies confirming former idea of early puberty onset linked to early menopause, but data from other studies are in contraversion, or finding no association. There are similarities and differencies in characteristics of these two periods. Both influence physical and mental health of women. An analysis of recent available data was done and presented in the paper.

Key words: puberty, menopause, reproductive transitions, hormonal regulation

Valedictory lecture

Estrogens, Estetrol and Breast Cancer

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Estrogens are known to stimulate the growth of existing estrogen-receptor positive BC, but estrogens are also an effective treatment of BC under special conditions. This contradictory knowledge is known as the "estrogen paradox". The data summarised in this presentation demonstrate that high-dose estrogens is an effective treatment of advanced breast cancer more than 5 years after menopause and also after the occurrence of resistance to endocrine anti-estrogen treatment. Essential for efficacy is an extended period of estrogen deprivation before the tumour is subjected to estrogen treatment (the "gap hypothesis). However, high-dose estrogens have been abandoned for BC treatment due to cardiovascular side-effects.

Estetrol (E4) may be a new treatment option for patients with advanced breast cancer, since this fetal estrogen has less interference with liver function and is expected to be less harmful for the CV system, whereas data from non-clinical and clinical studies suggest anti-breast tumor effects.

Currently, a phase IB/IIA, dose-escalation, safety and proof of concept study with high doses of E4 has been performed in Germany in postmenopausal patients with advanced ER+/HER- breast cancer. The study has been completed clinically and the preliminary anti-tumour and quality of life results will be presented, confirming the "Dual Efficacy" concept of high dose E4 in advanced breast cancer.

13th Annual Meeting of the Egon and Ann Diczfalusy Foundation

Abstracts of Posters

(In alphabetic order of the 1st author)

Female Infertility and abdomino-pelvic adhesions

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Infertility is the inability of a couple to conceive a pregnancy after 12 months of normal relations. In 25-30% of cases of female infertility are incriminated utero-tubal factors, from which the abdomino-pelvic adhesion are representing 10%. Adhesions are considered highly cellular vascularized and dynamic structures. Adhesion formation after surgery remaines an almost inevitable consequence of abdominal procedures. Studies have shown an incidence of adhesions around 95%. Also adhesions are appearing after pelvic inflammatory disease, most often determined by Chlamydia trachomatis or Neisseria gonorroeae. The chronic forms of this pelvic inflammatory diseases are creating peritubal and periovarian adhesions responsible for female infertility and also are creating adhesions in the abdominal cavity. Operative injuries and peritonitis are creating peritoneal mesothelial damages, peritoneal inflammation with the appeareance of fibrinous exudate bringing to fibrous adhesion formation. These processes are controlled by several cytokines produced by macrophages and fibroblasts, increasing the collagen synthesis, stimulating the adhesions proliferation. Multiple methods are used for adhesion reduction with variable efficiency. There is no one product that is currently avaible without certain drawbacks. Methods of adhesion reduction and the adhesion forming process are subject of research to avoid the appearance of infertility, ectopic gestation, chronic pelvic pain in female patients.

Malignant peritoneal mesothelioma with a long term postoperative survival - Case report

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Abstract

Malignant peritoneal mesothelioma is a form of cancer originating from the lining cells of the pleural and peritoneal cavities, as well as the pericardium and the tunica vaginalis. The incidence of malignant mesothelioma is increasing worldwide because of the use of asbestos. However, in Romania the asbestos-containing products that are installed or in service may be used until the end of their life cycle. This study reports a 34-year-old patient with a malignant mesothelioma of the peritoneum of foamy cell subtype, involving the omentum and left ovarian surface, where complete surgical cytoreduction seems to be a rational therapeutic approach, considering that there are no signs of relapsing tumour.

Keywords: malignant peritoneal mesothelioma, asbestosis, surgical cytoreduction

Introduction

Malignant peritoneal mesothelioma (MPM) is considered a rare form of intraperitoneal, aggressive neoplasm, strongly related to previous asbestos exposure [1]. Also it is considered as a form of cancer originating from the lining cells (mesothelium) of the pleural and peritoneal cavities, as well as the pericardium and the tunica vaginalis [2]. Its distribution may be uni- or multifocal or may involve the lining cells in a continuous manner [3]. Malignant mesothelioma of the peritoneal cavity accounts for only 10-20% of all mesotheliomas and usually involves elderly or middle age males, often with a previous history of asbestos exposure [4].

Epidemiology

Regarding the history of malignant peritoneal mesothelioma, we can see that before 1950, it was so rare that some pathologists even questioned its existence [5]. However, the incidence of malignant mesothelioma is increasing worldwide because of the use of asbestos after the Second World War as a building material. Although its use was widely abandoned in the Western world in the 1980s, the long latency period between exposure to asbestos and onset of mesothelioma, which can range from 15 to 60 years, meant that the mortality rates from mesothelioma have continued to rise [3:1,2].

In the 1960s a mesothelioma register was set up in the UK to record the mortality rates from mesothelioma and to try to identify the incidence of tumour development without known occupational exposure. It is predicted that around 90,000 deaths will occur from mesothelioma by 2050 [3:2; 6]. Manzini, in the clinical records of 15 patients affected by MPc, observed at the Monfalcone Hospital from 1982 to 2003, that asbestos exposure was present at 12 patients [1]. La Vecchia *et al* [7] used death certificates from 8 European countries to predict peak mortality between 2010 and 2020. Also a peak incidence in France is expected in 2030 [8] and is projected for 2012-2024 in Italy [9]. In Romania, by Government Decision (GD) of 15.04.2006 asbestos was outlawed, however GD no 734 / 2006 extended the

use of asbestos thus: "asbestos-containing products that have been installed or were in service before 1 January 2005 date may be used until the end of their life cycle ".

Clinical presentation

The studies on MPM report some limited series of single cases; in this condition, the initial symptoms on clinical presentation are poor, atypical, non-specific and the level of clinical suspicion is relatively low [10, 11]. Moore *et al,* consider mesothelioma primarily as a disease of adults, usually presenting in the fifth to seventh decades of life with 70–80% of cases occurring in men [3].

Manzini identified three different types of clinical presentation of MPM (sometimes assembled in different associations):

- the classical type - characterized by abdominal swelling due to ascites and/or an abdominal mass often associated with abdominal pain and weight loss, in 6 cases;
- the surgical type - characterized by a surgical emergency, in 5 cases;
- the medical type - characterized by fever, diarrhoea, weight loss, and acute phase reactant changes, in a clinical picture resembling that of intestinal inflammatory bowel disease, in 4 cases [1:1,2].

However, it is hard to make an initial diagnosis; this can be confirmed by accurate history, examination, imaging studies [3] and histopathological findings of hyaluronic acid level in the ascitic fluid [12].

Case Report

The 34-year-old patient, non-smoker, was admitted to the Gynecology Department of the County Emergency Clinical Hospital Oradea, Romania, with pain in the lower abdomen, weight loss, abdominal distension, ascites, and loss of appetite. The clinical examination highlights pale-earthly skin, muscular hypotonia, and ascites. The gynecology exam, manual vaginal exam and examination with valves highlight multiparous cervix (multigravida), with periorificial injury, and right adnexal mass.

The CT scan exam (Fig.1,2,3) reveal a large quantity of ascites, multiple intra-abdominal nodules sized 2-10 cm and a right ovarian mass. Moreover, the tumour marker CA 125 shows increased values. After these clinical and paraclinical findings, an ovarian neoplasm with ascites is suspected and surgical intervention is decided.

We are conducting a median pubo-supraumbilical laparotomy, and during the inspection of the peritoneal cavity a tumour mass of 10x9x7 cm is revealed, solid, friable, yellowish (like sulphur), cauliflower-shaped, with epiploic origin (which was the suspected right adnexal mass) and which invades the superficial cortex of the left ovary (Fig.4); moreover, multiple epiploic nodules are showing the same features, with the greatest diameter of 2.5 cm (Fig.5); we also found about 5 litres of ascitic fluid, a uterus of normal aspect and size, the right ovary with a normal aspect and a cystic left ovary. We performed an omentectomy, a partial resection of the left ovary, peritoneal biopsy and about 20 ml of ascitic fluid was collected for the cytology exam.

Figure 1. Imagine TC

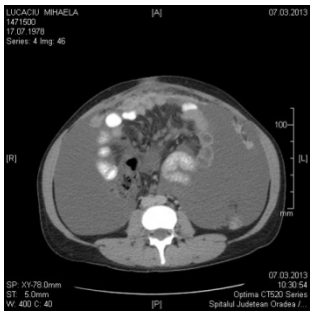

Figure 2. - Imagine TC

Figure 3. - Imagine TC

Macroscopical findings

Intraperitoneal multinodular tumour, with the biggest solid nodule of 10 cm in diameter, firm, rubbery, white-yellowish, with necrosis and other multiple omental nodules with the same features, with the diameter between 2,5 and 1 cm.(Fig.4,5)

Figure 4. - Intraperitoneal multinodular tumor, with the biggest solid, nodule of 10cm in diameter and multiple nodule with the same aspects with the diameter between 2,5 and 1cm

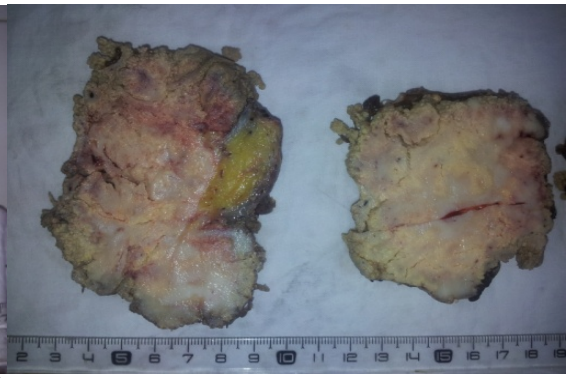

Figure 5. - Section of nodule with 10cm in diameter

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All the nodules previously described had the same morphology: architecturally, the tumour has a solid, papillary and tubule-papillary growth pattern, although small nests and cords of tumour cells may be seen. In contrast to serous tumours (which is the more frequent type of intraperitoneal tumour in women), the papillary pattern is non-hierarchical and cellular budding from the surface of the papillae is inconspicuous. The core of the papillae is often hyalinised and contains foamy histiocytes. The tubules usually are small and round. The tumour cells are of epithelial type, and retain a resemblance to mesothelial cells with a polygonal, cuboidal low-columnar shape, with moderate amounts of eosinophilic cytoplasm. Tumour cells with cytoplasmic vacuoles are sometimes present (Figure 6), focally suggesting an adenomatoid tumour. Mitotic figures are inconspicuous. Invasion of sub peritoneal tissue is present, the tumour dissecting into the omental fat. The stroma are prominent, from hyalinised to desmoplastic. Tumour necrosis is obvious. The immunohistochemical features are very helpful even if no single immunohistochemical stain is diagnostic. Positivity of tumour cells for Calretinin (Figure 7), Podoplanin and D 2-40, also negativity for p53 oestrogen receptors supports the diagnosis of malignant peritoneal mesothelioma.

Also, histopathological examination excluded the following lesions:

- atypical mesothelial hyperplasia (more commonly an incidental microscopic finding of a small solitary or multiple nodules; the mesothelial cells contain cytoplasmic vacuoles which stain for acid mucin); desmin-positive and EMA, p53 negative;
- reactive fibrosis (most commonly in desmoplastic malignant mesothelioma);
- well-differentiated papillary mesothelioma (often small, solitary, non-invasive; typically pure papillary pattern consists of fibrous cored papillae lined by a single layer of benign-appearing, mitotically inactive mesothelial cells);
- adenocarcinoma with diffuse peritoneal involvement, including metastatic serous adenocarcinomas and serous carcinomas of primary peritoneal origin (histologically, the serous tumour presents a complex papillary pattern, with the papillae containing fibro vascular cores, covered by stratified epithelial cells and cellular buds, often with single cells exfoliating from the papillae; mitotic figures are conspicuous, marked nuclear atypia; psammoma bodies occur frequently; p53+ immunoreactivity; serous carcinomas are usually immunoreactive for MOC-31, Ber-EP4 and oestrogen receptors; positivity for calretinin, CK 5/6, podoplanin and D2-40 favours peritoneal malignant mesothelioma).

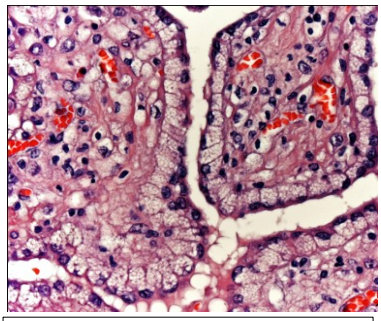

Figure 6. Mesothelioma H-E

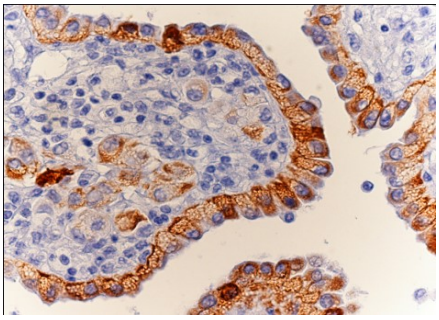

Figure 7. Mesothelioma IHC: CK5/ 6

After a clear diagnosis of malignant mesothelioma of the peritoneum involving the omentum and left ovarian surface was made, we conducted an epidemiological investigation. We found that the roof of the patient's house was made of asbestos cement boards, corroded, patient collecting water rain drain on them for domestic use, being constantly exposed to inhalation of asbestos particles. The patient was directed to oncology services, but unfortunately she declined any further oncological treatment.

Seven months after the surgical intervention, the patient presented to the Gynecology Department of the County Emergency Clinical Hospital Oradea, Romania, with a generally altered state, the clinical examination revealing umbilical hernia, abdominal distension, ascites, modified bowel habits; taking into consideration the diagnosis of malignant peritoneal mesothelioma, it was decided to perform another surgery, for a 'second look' and for surgical cytoreduction after having conducted a thorough preoperative preparation.

We conducted a median iterative pubo-supraumbilical laparotomy. During the examination of the peritoneal cavity, almost 2 litres of ascitic fluid were collected for cytology; we also found adhesions of the recto-sigma to the left adnexa, intestinal loops to the parietal peritoneum and the caecum to the uterus. After the extensive adhesiolysis, the full hysterectomy was performed with a bilateral salpingo-oophorectomy. After the examination of the pelvic peritoneum, a tumour mass, of approximately 1 cm diameter is observed at the bottom of the Douglas pouches, which is removed. Moreover, we perform a lymphadenectomy to an external iliac lymph node, to a right obturator lymph node and the extirpation of a retrocrural tissue. In the next step we examine the parietocolic gutters, both diaphragmatic cupolae are being examined and palpated as well as the surfaces of the spleen and the liver. Because of

the high risk of pneumothorax, no peritoneal biopsy was performed from the right hemydiaphragm and there have been no macroscopically identified abnormalities. In order to continue the process, the colon was examined next, from the rectum to the caecum, removing a perirectal tumour of approximately 7/5 mm. Examining the small intestine, from the ileocaecal valve to the Treitz ligament, we did not find any suspicious macroscopical abnormality. A mesenteric tumour approximately 1 cm diameter was removed. Moreover, we perform an omphalectomy.

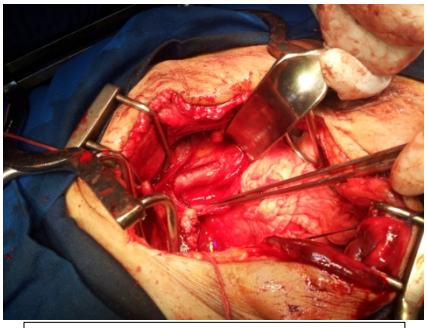

Figure 8. - Intraoperative view

The microscopical examination reveals the tumour proliferation in the following fragments: a perirectal tumour (7x5 mm node), peritoneum (diffusely infiltrated with a tumour of 5x5 mm), a mesenteric nodule (epiploic appendix of 10/6 mm), the serosa of the uterine corpus at the bilateral adnexa (serous tubal, the surface of the ovary and the superficial cortex – infiltrated); the cutaneous fragments sent separately and the umbilical scar being coated thoroughly by the peritoneal serosa, diffusely infiltrated by the tumour cells with the aspect of malignant mesothelioma. The pelvic lymph node: one in the right external iliac area and one in the right obturator area reveal a sinus histiocytosis; the retrocrural tissue – fat. Cervix: chronic cervicitis and endocervical microglandular hyperplasia without atypia. Uterine corpus: endometrium in the mid proliferative phase. Adenomyosis. Uterine serosa infiltrated with tumour cells. Adnexa: bilateral ovarian cystic follicles and the superficial cortex infiltrated with tumour cells; the left ovary present a foreign-body giant cell reaction.

In March 2015, the patient was admitted to the surgical department with a generally altered state, accusing generalised abdominal pain, nausea, vomiting, postoperative eventration strangled by necrotic tissue at the eventration site and the lack of bowel transit. After a clinical and paraclinical analysis and an appropriate preoperative preparation, on the 12th of March 2015 we performed another intervention and found a generalised faecal peritonitis, the necrosis of an ileal loop in the eventration pouch and extensive adhesions syndrome. After the removal of the necrotic ileal loop with the LL, an ileoileal anastomosis and the cure of the monoplane eventration, the postoperative evolution has been disappointing, calling for another exploratory intervention on the 20th of March 2015, when we found skin necrosis along with fixed evisceration, an anastomotic fistula and obstructive faecal peritonitis in pelvis. The anastomosis and ileostomy were performed, after which a Pezzer's catheter was introduced in the ileostomy, being ultimately removed. At the histopathological examination in the sections analysed, there is necroinflammatory activity on the serosa of ileum with a rich inflammatory polymorph infiltrate, fibrin deposits, granular tissue and unspecified granulomatous inflammatory reaction. In the examined fragments, in the usual H-E coloration, there cannot be seen any tumour cells.

On 12th of September 2015, the patient presents at the surgery department for a check-up and after the clinical and paraclinical examination, no signs of relapsing tumour were found.

On July 2016, the patient returns for a clinical evaluation, examination showing a good general condition without any clinical signs of relapse.

Conclusions

It is difficult to diagnose malignant peritoneal mesothelioma diagnose preoperatively because it can be easily confused with *an ovarian tumour*, a thickening of the peritoneum and of the mesentery, the presence of the intra-abdominal multiple nodules and ascites not being characteristic. Complete surgical cytoreduction seems to be a rational therapeutic approach in the case of the malignant peritoneal mesothelioma.

Conflict of interest

The authors declare no conflict of interest.

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Hematohydrohysterocolpos with vaginal atresia - Case report

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Abstract

Hydrocolpos is a rare condition, clinically obvious at birth, or within the first few weeks of life and it appears as an abdominal mass associated with the absence or abnormality of the vaginal opening. A premature 25 days old female new-born was diagnosed with hematohydrohysterocolpos, imperforate hymen. After the surgery, the evolution is positive and the patient is released from the hospital in a good general state.

Keywords: imperforate hymen, vaginal atresia, hematohydrohysterocolpos of a newborn

Introduction

Hymenal anomalies result from incomplete degeneration of the central portion of the hymen. Variations include imperforate, microperforate, septate, and cribriform hymens. Although most of these variants are not clinically significant, hymenal anomalies require surgical correction if they block vaginal secretions or menstrual fluid, interfere with intercourse, or prevent treatment of a vaginal disorder.

Imperforate hymen represents a persistent portion of the urogenital membrane. It occurs when the mesoderm of the primitive streak abnormally invades the urogenital portion of the cloacal membrane. It is one of the most common obstructive lesions of the female genital tract. When mucocolpos develops from accumulation of vaginal secretions behind the hymen, the membrane is seen as a shiny, thin bulge. The distended vagina forms a large mass that may interfere with urination and at times may be mistaken for an abdominal tumor. Topical anesthetic is used to prevent discomfort to the newborn, and the central portion of the obstructing membrane is excised. When imperforate hymen is corrected in infants, the central portion of the membrane is excised; sutures usually are not necessary.

If missed during the newborn period, imperforate hymen often is not diagnosed until an adolescent presents with complaints of primary amenorrhea and cyclic pelvic pain. It may present as back pain or difficulty with defecation or urination secondary to mass effect from vaginal distention. Inspection of the vulva may reveal a purplish-red hymenal membrane bulging outward as a result of accumulation of blood above it (hematocolpos). Blood may fill the uterus (hematometra) and spill through the fallopian tubes into the peritoneal cavity. Endometriosis and vaginal adenosis are known but not inevitable complications.

Repair of imperforate hymen is facilitated if the tissue has undergone estrogen stimulation and the membrane is distended. When the procedure is performed in an adolescent, a large central portion of the membrane should be removed because the edges of a small incision may coalesce, allowing the obstructing membrane to reform.

Hydrocolpos is an anomaly and a rare condition which occurs in new-born female infants as the result of the stimulation of maternal estrogens; it consists of atresia of the vaginal outlet and excessive secretion of the cervical glands and produces a midline mass and building at the introitus.

Regarding the etiology, we find two theories in the academic literature, both of which may be regarded as correct:

- an imperforate hymen, which is the true cause;
- a thick membrane is responsible for it (considered to represent an atresia, similar to that of imperforate anus)

Hydrocolpos is clinically evident at birth, or within the first few weeks of life, and it appears as an abdominal mass associated with absence or abnormality of the vaginal opening. The diagnosis is confirmed by abdominal ultrasound and CT scan.

Females with vaginal atresia lack the lower portion of the vagina, but otherwise have normal external genitalia. The embryonic origin of this condition is presumed to involve failure of the urogenital sinus to contribute its expected caudal portion of the vagina (Simpson, 1999). As a result, the lower portion of the vagina, usually one fifth to one third of the total length, is replaced by 2 to 3 cm of fibrous tissue. In some individuals, however, vaginal atresia may extend to near the cervix.

Since most women with vaginal atresia have normal external genitalia and upper reproductive tract organs, this condition does not often become apparent until the time of expected menarche. Adolescents generally present shortly after physiologic menarche with cyclic pelvic pain due to hematocolpos or hematometra. On physical examination, normal breast and pubic hair development is present. The perineum is usually normal, with normal secondary sex characteristics with a hymeneal ring and beyond the ring, a vaginal dimple or small pouch. A rectoabdominal examination confirms the presence of midline structures. Additionally, sonographic or MR imaging will display upper reproductive tract organs. Of these, MR imaging is a more accurate diagnostic tool, as the length of the atresia, the amount of upper vaginal dilatation, and the presence or absence of a cervix can be identified. Laparoscopy, however, is necessary for diagnosis when the anatomy cannot be fully evaluated with radiographic studies. For example, Economy and associates (1998) reported that MR imaging has only 31-percent sensitivity for the detection of uterine structures in patients with vaginal agenesis. About one third of women with vaginal atresia have associated urologic abnormalities.

Vaginal atresia is distinct in clinical and embryonic characteristics from transverse vaginal septum. In patients with transverse vaginal septum there is a well-developed vagina in which a thick intervening septum separates the lower from the upper vagina. Conversely, in those with vaginal atresia, fibrous tissue develops in place of the vagina. In some, nearly the entire span beginning at the perineum and extending cephalad to the cervix may be fibrotic. Identification of the cervix in such cases distinguishes vaginal atresia from mullerian agenesis.

Case Report

A premature new-born female, 25 days old, is admitted in the paediatric unit for the bio-clinical re-evaluation and a specialised treatment, having previously been diagnosed with congenital pelvic tumour.

The medical history of the illness reveals that starting from the intrauterine life, affirmative, a tumour mass is being observed via ultrasound - approximately 5 cm in diameter, situated in the abdominal cavity, right next to the uterus, interpreted as a cystic ovarian tumor by the obstetrician. Postnatally, the new-born presents a good general state, with a balanced respiratory and cardiovascular function, present bowel transit, present diuresis. At the ultrasound check-up, the presence of a tumour mass in the intra-abdominal cavity is confirmed, having a mixed parenchymatous-fluid aspect, hard to appreciate as being part of the organ.

In order to identify the nature and the origin of this mass, a CT scan is being performed that shows images suggesting a cystic pelvic-subperitoneal mass. It is important to mention that

the examinations conducted in the laboratory have not highlighted any alterations of the renal function.
The general clinical examination reveals a voluminous distended abdomen which highlights a tumour mass in the hypogastrium with the palpation of a firm mass, adherent to the subjacent plans, painless, unique, of 6/7 cm dimension.

Figure 1. - Abdominal pelvic tumor size

The abdominal ultrasound highlights a space occupying abdominal-pelvic process, with fluid content, a possibility of an increased volume of the uterus, with difficult limits to set, with hematocolpos and bilateral hydro nephrosis with secondary compression. A specialised team, comprised of a surgeon and an oncologist, decide the timing of the procedure in order to precisely establish the affected organ through MRI studies. The images provided by the MRI advocate for a giant fluid abdominal-pelvic mass with (most probably) uterine connections and secondarily bilateral hydro nephrosis.

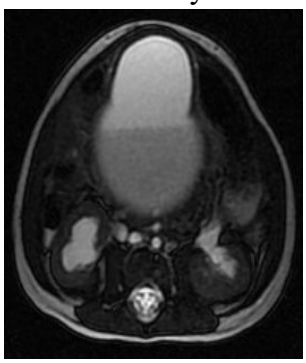

Figure 2. – MRI Section

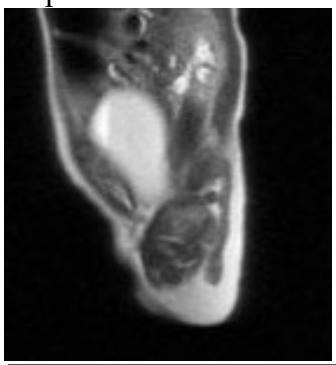

Figure 3. – MRI Section

Figure 4. – MRI Section

The laboratory examination revealed the changes: increased levels of Lactate dehydrogenase (LDH) – 267u/l, AFP alpha-fetoprotein 486.64 ng/ml, total serum proteins 5.35 g/dl, serum creatinine 0.20 mg/dl and a decrease in urea nitrogen 9.27 mg/dl.
As a result of these investigations, clinical and paraclinical, after the gynaecological examination which highlights the imperforate hymen, we set the diagnosis of hematohydrohysterocolpos, imperforate hymen and after a thorough preoperative preparation, we performed the surgery. A No 18 needle was inserted into the membrane at the introitus, and 20 ml of haematic, brownish liquid was removed, when we observed a vaginal atresia. Then, on needle path, we performed a straight and deepness incision of approximately 1 cm at the introitus membrane, at a distance from the urethra, bladder and the rectum in order to not sever them. On the colpos incision, we evacuated about 200 ml of haematic, brownish liquid.

At the end, a drainage tube was fixed through the incision in order to ensure the complete evacuation of the intraperitoneal content, which was removed after 7 days.

Figure 5. – Intraoperative view

Figure 6. – Intraoperative view

Figure 7. – Intraoperative view

Figure 8. – Ultrasound after surgery

The follow-up abdominal ultrasound performed in the first day after the surgery highlights an decreased of the bilateral hydro nephrosis from stage II, prior to the surgery, to stage I - a uterus significantly reduced in size, without any fluid in it. Under antibiotic cover the evolution is positive and the patient is released from the hospital in a good general state 10 days after surgery. After this, the child is being periodically followed up to monitor normal subsequent development of the genitalia.

Figure 9. - The ultrasound performed 2,5years after surgery.

Conclusions

The imperforate hymen and/or atresia of the distal vagina can be caused by fluid and blood successive to the genital crisis of the new born baby so that the hematohydrohysterocolpos to produce pseudo cystic pelvic tumors susceptible to compress both ureters leading to hydronephrosis.

The advisable/opportune surgical treatment that involves the evacuation has, including, the fetal vital indication.

Conflict of interest

The authors declare no conflict of interest.

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Abortion – still a pathological contraceptive method for Romanian people

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Introduction: Romania had the highest maternal mortality in Europe especially due to unsafe abortion and prohibition of the contraceptive methods during the communist regime. In the 30 years that followed, still abortion represents a contraceptive method for Romanian population, although Romania is a member of the European Union and now contraceptive methods are available on a large scale.
Material and method. A statistical comparison of the two periods will be performed based on the official data received from the Public Health Authorities.
Results. For the period 2013-2016, there were 3068 abortions performed, out of which 2749 were performed on the patients request. 16 abortions were performed in unsafe conditions and the rest were represented by incomplete abortions. 35-38% of the TOP performed on the patients request were done in private medical facilities. Persons with more than 5 abortions were registered frequently; most of these procedures being asked for by the age group 30-34 and 35-39 years old. Majority of TOP were performed by dilation and curettage technique.
Conclusions. The rates of abortion in Romania are one of the highest in Europe and the way of performing it can generate a lot of complication (D&C method). Official data is scarce regarding abortions as not all private facilities need to declare this procedure. As persons appeal several times for TOP, we conclude there is a poor contraceptive education and abortion is still considered a contraceptive method.

Keywords: abortion, contraception, termination of pregnancy (TOP)

AMNIOTIC FLUID VOLUME – A POSSIBLE PREDICTOR OF FETAL OUTCOME IN PPROM?

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Rupture of membranes before term is one of the most frequent factors involved in the process of giving birth before 37 weeks of pregnancy. This study aimed to investigate the benefits of ultrasound assessment of amniotic fluid in patients admitted with preterm rupture of membranes in predicting immediate neonatal clinical and paraclinical outcome.

A database was created collecting information on maternal status at the time of admission, ultrasound pregnancy evaluation and fetal paraclinical markers determined immediately after birth. Results showed that 29% of 217 patients admitted in 2018 in our clinic with ruptured membranes had less than 37 weeks of pregnancy. The analysis of amniotic fluid objective quantification and the number of hours of ruptured membranes resulted in a Pearson correlation coefficient $r = 0.27$, showing no statistically correlation between these variables.

Correct management of patients diagnosed with preterm ruptured membranes is still a matter of concern in our clinic since approximately 5% of all births in 2018 were accounted in this group; consistency in objective measurement of amniotic fluid aims to be better implemented.

Keywords: preterm, rupture of membranes, CRP, respiratory distress, infection

The outcomes of triplet pregnancies

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Introduction: The wide use of assisted reproduction has resulted in 4- to 5-fold increase in the incidence of triplet pregnancies, which carry an extremely high risk of maternal complications and adverse perinatal outcome.
Aim: The aim of the study was to present maternal complications and perinatal outcome of triplet pregnancies.
Methods: The study population consisted of triplets delivered between January 1st, 2010 and January 1st, 2015 at the Department of Gynecology and Obstetrics, Clinical Center of Vojvodina in Novi Sad.
Results: Of the 55 cases of triplet pregnancies, the average maternal age was 32 years in the study period. The average BMI was 30.56. There were 7 (12.72%) spontaneous triplet pregnancies in the sample, while the pregnancies conceived by IVF procedures were 44 (80%) and 4 (7.28%) were post-insemination pregnancies. The average gestation at which the pregnancy ended is 33.2 gestational weeks (25-37). The birth rates of ≤28 gestational weeks and ≤32 gestational weeks were 9.1% and 38.2%. 54 (99.18%) pregnancies were completed by Caesarean section, while only one patient underwent vaginal delivery. The average blood loss was 1000ml,
there were no hysterectomies. The most common maternal pregnancy-induced complications
Were anemia (74.55%), hypertension (38.18%), thrombophilia (25.45%), obstetric cholestasis (34.55%) and gestational diabetes (9.1%). Preterm premature rupture of membranes was observed in 11 (20%) cases (27-34 gestational weeks). Prophylactic cerclage was set in 34 (61.82%) pregnant women, and in 35 (63.64%) cases Dexasone therapy was administered. The average birth weight of children with the first baby was 1865g, with the second 1769g, and with the third 1697g. Body weight ≤1000g for all three newborn of triplets was observed in 16 (29%) cases. The mean AS in the first minute was 7, while in the fifth minute it was 8.
Conclusions: Maternal and especially neonatal risks in triplet pregnancies should be carefully considered before counseling for the continuation of multiple pregnancies. The implementation of single embryo transfer (SET) leads to a reduction in rate of multiple pregnancies after IVF procedures and the attendant complications, without compromising IVF success.
Keywords: Multiple pregnancies, complications, perinatal outcomes, single embryo transfer.

Postpartum contraception – incomplete knowledge of opportunities

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Objetive: Postpartum contraception is an important part of gynecology. After giving birth, womens' body needs recovery time which should be at least twelve months. In spite of the large selection of contraceptive methods in Hungary, significant part of women don't know the possible ways of protection against unwanted pregnancy. The aim of our study was to assess 1) the contraceptive habits and knowledge of women who have given birth at least once and 2) how well informed are doctors and lawyers of the future about contraception in general and in the area of postpartum contraception.

Methods and design: In the study took part 180 medical students, 80 from the third and 100 from the fifth year (before and after learning gynecology), 83 law students and 143 women aged between 17 and 43 years who gave birth at least once. We assessed the partricipants knowledge with a questionnaire, in which we asked about contarceptive methods. Adult women were also asked about their pregnancy. The results were inserted into an electrical database and the datas were analysed with SPSS 23.0 using descriptive statistics and khi square test.

Results: According to our research, only 11.2% of the participating women are familiar with all of the methods listed, 34.3% knows five or less methods. There was a significant correlation between the number of known contraceptive techniques and the highest level of education. More than half (55.2%) of the mothers did not receive information on contraception after giving birth. The survey also shows that most women prefer aborted sex, condoms and birth control pills before and after childbirth. On the basis of the response of the students of the Faculty of Medicine, students in the fifth year (on average = 9.9) know more methods than the students in the third year (mean = 7.8). Law students know even less about contraception (mean = 6.8). Most of the research participants consider rubber condom, contraceptive pill and spiral as the safest methods. The majority are not aware of the contraceptive effect of breastfeeding. Those who think that breastfeeding protects against unwanted pregnancy do not know the mechanism and its conditions.

Conclusion: Based on the results, we can say that neither mothers nor university students have adequate knowledge of contraception. Therefore, it can be concluded that all target groups would needed more detailed information on general and postpartum contraception.

Highschool female student's awareness about cervical cancer risk factors

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Introduction: HPV infection is the most common cervical cancer risk factor. There is a great importance of high school student's education about reproductive health.

Aim: to examine female high school student's knowledge about HPV infection, cervical cancer risk factors and to spread knowledge about importance of preventive exams.

Materials and Methods: research was conducted by self-constructed questionnaire among 170 highschool female students.

Results: we examined 170 students aged 15 to 19 years at average 16,6 years. Our sample were students of Medical (41,2%), Economics (21,4%) and Grammar (21,4%) high school. From respondents 12,3% is sexually active. More than a half students (52%) use condom as contraception. Half of respondents knew about Pap smear, and only 34,1% heard about HPV infection. Students know HPV infection causes genital warts (13,5%), and cervical cancer (46%). Seven out of ten students don't know anything about symptoms of HPV infection, and only 13% of students heard about HPV vaccine. As most important risk factors for HPV infection and cervical cancer students recognize: number of sexual partners and young age. Almost all students (97%) are motivated to take up lectures about cervical cancer risk factors and HPV infection.

Conclusions: there is a serious need for education about cervical cancer risk factors, and HPV infection among high school female students. Also, there is a great need to popularize routine preventive exams.

Keywords: HPV infection, Highschool students, Knowledge

The hidden indications of cesarean section on request- a 3 year retrospective study regarding the real situation of cesarean in Arad Maternity Clinic

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Introduction: Cesarean section is the most common obstetrical surgical procedure and it can be a life saving procedure, but also it can create a series of complications if it is performed without a proper indication. Cesarean section rate proposed by WHO is 15%, but it Romania, in most county hospitals it exceeds 50% and almost all have an emergency situation indication for it.

Design & Methods: A retrospective study was conducted for the period 2016-2018 in Emergency Arad County Clinical Hospital regarding the cesarean sections performed, with a closer crossed analysis of the doctor performing the procedure and its indication for it, but also other parameters that could lead or influence it.

Results: 3540 cesarean files were studied. The outcome of them showed good results for both mother and the baby in the frame of the data in the literature or other studies performed in this maternity department. The doctors performing cesarean were placed in 3 groups depending on the number of cesareans performed and their main indications for cesarean section were determined. The analysis revealed much higher rates for atypical indications compared with the literature and a planning of them although they had emergency indications.

Conclusions: Cesarean section performed on the request of the patient or because of the commodity of the doctor or its fear of malpractice is a common situation in Romania and our research proves that ~ 50% from the total of the cesareans performed in Arad Maternity Clinic can be treated as such. Further measures are needed to prevent such facts and to determine future mothers to deliver natural and not expose themselves to the complications the cesarean section can generate.

Key words: cesarean section, malpractice

THE ASSOCIATION AMONG CERVICAL, ANAL, AND ORAL HPV INFECTIONS IN HIGH-RISK AND LOW-RISK WOMEN

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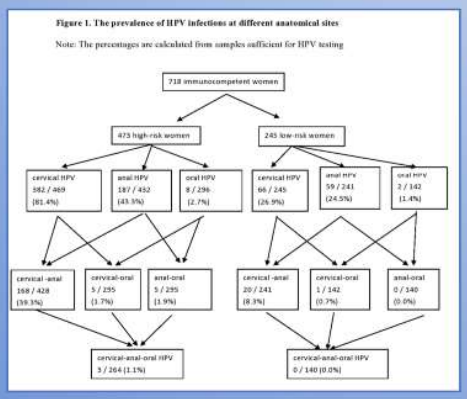
Background:

The human papillomavirus (HPV) can cause premalignant and malignant tumors in the anogenital and oropharyngeal regions.

Methods:

A total of 718 immunocompetent women were enrolled in the study. The high-risk (HR) group consisted of 473 patients with biopsy-confirmed high-grade cervical lesion while the low-risk (LR) group consisted of other 245 women. All participants completed an anonymous self-administered questionnaire and were subjected to cervical, anal, and oral HPV genotyping using the Linear array HPV test.



Basic subject characteritics		Low-risk group N = 245	High-risk group N = 473	P[1]
Age (years)		40.0 (25.0; 62.0)	33.0 (23.0; 58.0)	< 0.001
Number of pregnancy		2.0 (0.0; 5.0)	1.0 (0.0; 4.0)	< 0.001
Number of births		2.0 (0.0; 3.0)	1.0 (0.0; 3.0)	< 0.001
Hormonal treatment		73 (29.8 %)	199 (42.1 %)	< 0.001
Autoimmune diseases		29 (11.9 %)	41 (8.7 %)	0.185
Smoking		76 (31.0 %)	216 (45.7 %)	< 0.001
No condylomata acuminata		191 (78.0 %)	386 (81.8 %)	0.432
Coitarche < 16 let		33 (13.5 %)	103 (21.8 %)	0.016
Number of sex partners < 3		45 (18.4 %)	47 (10.0 %)	0.006
Unprotected sex		220 (89.8 %)	429 (90.7 %)	0.505
Non-coital contact - anus		157 (63.9 %)	334 (70.7 %)	0.201
Anal sex		70 (28.6 %)	190 (40.2 %)	< 0.001
Education	elementary school	72 (29.4 %)	138 (29.4 %)	0.900
	high school	108 (44.1 %)	200 (42.6 %)	
	college	65 (26.5 %)	132 (28.1 %)	
Anamnesis of conisation (last 1 year)		13 (5.3 %)	17 (3.6 %)	0.325
Oral sex		223 (84.8 %)	448 (90.7 %)	0.188

Results:

A total of 81.4 % women were infected in the cervix, 43.3 % in the anus, and 2.7 % in the oral cavity in the HR group in comparison with only 26.9 %, 24.5 %, and 1.4 % in the low-risk LR group, respectively. The cervical and anal HPV infections were much more frequent in the HR patients ($p < 0.001$); the difference in the oral HPV prevalence was not significant ($p = 0.511$) between groups. Concurrent cervical-anal infection was observed in 39.3 % of HR women and in 8.3 % of the LR patients ($p<0.001$) and it significantly increased with the grade of cervical lesion ($p_{trend}<0.001$). The higher prevalence of concurrent cervical-oral, anal-oral, and cervical-anal-oral infections in HR women was statistically not significant according to the generally small oral HPV prevalence.

Conclusions:

All HPV infections occurred more often in HR than in LR women but not all results were statistically significant. The genotype HPV 16 was found in approximately half of all infections at all sites.

I would like to express my thanks to my fellow colleagues from NNB, especially to Dr Sehnal for his aid and support in sample collections.

Maternal care of Roma pregnant women in Arad County

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Introduction: Social marginalization, male involvement and the role health institutions play in shaping women's care-seeking behavior needs further attention in gaining access to maternal health care. Due to inadequate reproduction policies in Romania, the levels of maternal mortality are ones of the highest in Europe. Additionally, the lack of prenatal examination increases this rate even more.
The aim of the project is to improve the awareness of, access to and quality of preventive and curative health services with a view to reducing infant mortality and morbidity, maternal mortality and morbidity, by providing pre and postnatal care amongst Roma communities in the County of Arad.

Material and methods. It is a collaborative project: White ribbon Alliance for safe motherhood Sweden, Networks Arad Romania, Department of Obstetrics and Gynecology, Vasile Goldis University Arad Romania, Karolinska Institute and University Hospital, Stockholm Sweden. The study will include as well as a qualitative design study: In depth-interviews with Roma pregnant women who will be interviewed about their and their children's health, social situation and quality of life. Their husbands/partners and caregivers will also be interviewed and the quantitative design study will be represented by a medical questionnaire containing medical history and pathology, and social status.
Results. The expected results will increase our knowledge in global health about how social marginalization and the role health institutions play in shaping care-seeking behavior, as well as highlighting high risk pregnancies and their management. It is estimated that results will provide new insights on what factors are important for Roma minority pregnant women in accessing maternal care in both emergency and sustained situations.
At last but not at least, it is in line with the UN statement of the 2030 Agenda for Sustainable Development.
Conclusion. Improving pre and post natal care in Roma communities in order to decrease maternal and child mortality and morbidity.

Years of life adjusted by PAP screening

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Introduction: The PAP test is very effective in screening for cervical cancer. For assessing the benefits that this method brings to society by increasing the quality of women life and survival, the QALY evaluation method has been used. QALY represents the adjusted/improved life year by a health measure and takes into account both the quantity and quality of life that is improved by medical intervention.
Design & Methods: Were analyzed comparative cases tested by PAP method and cervical cancer cases in Arad County using the QALY methodology. 2 study batches were formed, one of 10,141 cases evaluated by Pap cytology between 2008-2017 and the control group with 1,033 cervical cancer cases from the same period, which did not benefit from the PAP screening. The cases were extracted from the general database of the Emergency County Clinical Hospital in Arad.
Results: PAP Screening has increased the years of life adjusted to all age categories compared to oncological therapy. The PAP carried out on 10,141 women has ensured survival of 10 years compared to the 5-year survival of the 1,033 women treated oncologically with a cost of 4.71 times lower.
Conclusions: As with other countries strategies, cervical cancer screening is required after the age of 20, for the decade of 20-30 years being the highest earnings of quality of life, gains that are maintained until the age of 70.

Cervical cancer screening in Arad County, Romania between 2008-2017

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Introduction: Cervical cancer is a severe condition, but detection in non-invasive stages leads to the prevention of mortality. Early detection and appropriate treatment are possible only if there is a robust screening program.

Design & Methods: A retrospective study was conducted and comparative cases have been studied in the case of cervical cancer screening in Arad County before and during the National Program.

Results: 10,141 Women were tested, 4263 (2.01%) in the first 5 years of this decade and 5878 (2.77%) in the second half of the decade, which corresponds to the national Cervical Cancer Screening Program in Romania. Of the total 10,141 women tested in 247 cases (2.44%) there were atypical type of ASC or AGC; 334 (3.3%) were Koilocytosis (LSIL); 204 were HSIL (2.01%), and 22 cases were neoplasms (0.21%). The mean age of ACG cases is 43 years, ASC-H, ASC-US and H-SIL lesion occur frequently over 45 years and the mean age of cases with cervical cancer (n = 22) is 56 years. Only 7.19% of the population eligible for cervical cancer screening performed this PAP test in a 10-year period.

Conclusions: Cervical cancer Screening is helpful in the survival of patients identified with precancerous and cancerous lesions, with evident results more favorable with the initiation through the health Program.

Uterine rupture at the Clinic for Gynecology and Obstetrics of the Clinical Center of Vojvodina

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Introduction: uterine rupture and placental abnormalities represent two most serious complications in obstetrics leading to high maternal and neonatal morbidity. The number of cases is increasing in parallel with the number of cesarean sections. Raising question is how the healing of the uterus depends on the way of the uterus suturing.
Aim: to determine frequency and perinatal outcome in patients with uterine rupture.
Material and methods: retrospective study of uterine rupture cases at the Clinic of Gynecology and Obstetrics of Clinical Center of Vojvodina from 2007 - 2018.
Results: in investigated period 2007- 2018 there were 77.218 total deliveries, 22.966 cesarean sections, 216 uterine ruptures. Age of patients was 31.5 years in average. Most of the cases of uterine rupture were asymptomatic, noticed during elective cesarean section (53.5%). Different terminology was used to describe asymptomatic rupture of uterus - silent rupture, scar dehiscence, incomplete rupture. Rupture occured most frequently in second pregnancy, in patients with at least 1 uterine scar and when the time distance from the previous cesarean section was 2 years. In vaste majority of the cases cesarean section was done in term (93.4%) with average blood loss of 673.5 ml (100-3000ml).
Conclusion: prevalence of uterine rupture is increasing. Risk factors for uterine rupture are uterine scar and shorter period from the last cesarean section. Neonatal complications are rare, whereas uterine rupture causes maternal complication in current delivery and future pregnancies.

Keywords: uterine rupture; cesarean section.

Antenatal perineal training for injuries prevention: follow up after puerperiom

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Introduction: Literature reports that 21% of women, 24% reported dyspareunia at 6 months postpartum stress urinary incontinence, overactive bladder syndrome, pelvic organ prolapse and fecal incontinence. These are the first results of an ongoing multicentrum study to investigate the effects about a correctly preparation to birth to prevent perineal trauma.

Materials and methods: The sample is represented by a experimental group of 56 primiparous women from 25 to 48 years old, to them different methods of childbirth preparation have been presented to allow a informed/awared choise. The proposed methods include Perineal Massage (PM) or training with Perineal Baloon (PB); both methods have been illustrated in ambulatory setting with specific instructions. The control group is composed by women who didn't apply any preparation method of perineal preparation to birth.

Results: From a sample of 56 women, 27% have applied the PB, 32% the PM and 41% haven't used any preventive treatment. The analysis shows that PB decreases episiotomy incidence and prevents perineal tears, 86% of them didn't receive episiotomy and only 26% presented pelvic floor dysfunctions as dyspareunia, urinary incontinence and vaginal prolapse. About perineal massage, the rate of perineal tears and dysfunctions increase appreciably.

Conclusions: From the study emerged that an adequate perineal preparation during pregnancy decreases the risk of perineal trauma, it also reduces episiotomy treatment and pelvic floor dysfunctions after vaginal birth. Authors believe that the study can be a initial step to develop an applicative method also in-hospital setting to reduce iatrogenic damages due to vaginal birth.

Treatment of postpartum vaginal relaxing with dyspareunia: PFMT vs vibrating vaginal cone

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Purpose: After childbirth, women may present pelvic floor disorder which may promote comorbidities and have an adverse effect on *quality of life* (QoL). During the puerperium, Pelvic Floor Muscle Training (PFMT) can treat and prevent these conditions and increase QoL [2]. For increased efficacy, PFMT can be combined with vaginal devices such as cones [3].

The aim of the study was to compare the efficacy of the *vaginal cone* (VC) versus traditional PFMT in the treatment of women presenting perineal muscle relaxing and sexual dysfunction after delivery.

Materials and methods: The VC had a novel physiological shape within which a steel ball was loosely-contained in order to generate vibrations against the cavity walls during exercises [Fig. 1]. A randomised comparative study was conducted on 57 women during puerperium; the study group used the VC while the control practiced traditional PFMT. A gynaecological examination was conducted 3(T0) and 6(T1) months after delivery.

Results: Pc test showed a significant increase in every parameter for both groups (T0-T1) [Fig. 1]. However, a FSFI questionnaire revealed significant improvements in satisfaction and pain in the study group vs the control [Fig. 2]. Furthermore, the study group exhibited a 95.4% decrease in dyspareunia compared to a 37.5% in the control group (T0-T1) [Fig. 3]. Numerous additional gynaecological benefits were observed when using the VC versus traditional PFMT and 87.5% of women were satisfied with its comfort and ease of use.

Conclusion: VC should be considered an efficacious device to treat perineal relaxing and associated sexual disorders during the puerperium.

The association between obesity and bone mineral density among 40-80 years old hungarian population

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Objective: Obesity has become a global epidemic problem. According to the report of the World Health Organization, obesity has nearly tripled since 1975. Obesity is a risk factor for several deseases, for example musculosceletal problems and increases the prevalence of fractures. Bone mineral density (BMD) declines with age leading to osteoporosis and bone fragility. According to the international literature high Body Mass Index (BMI) is negatively assoiated with BMD. The aim of this study was to assess the relationship between BMI and BMD among hungarian men and women.

Design and methods: Altogether 725 participants (321 men and 404 women) took part in the OTKA NN110932 study in South Hungary in University of Szeged, Faculty of Medicine, Department of Obstetrics and Gynecology. We measured body weight and height and calculated BMI. BMD was measured in the calcaneus bone. We divided the participants into 8 groups by sex and age. For the statistical analysis we used SPSS 24 program and performed descriptive and correlation statistics and analysis of variance.

Results: The mean BMD value at men is 0,488 g/cm^2 and at women 0,420 g/cm^2. The mean values of BMI at men is 29,4 kg/m^2 at at women 28,4 kg/m^2. We found a positive, significant relationship between BMI and BMD at both sexes even after adjusting for age.

Conclusion: Our results do not correlate with the reviewed literature. The assessed population is overweighted and BMD does not show a decrease with increasing BMI. Further investigations are needed after orientating about the vitamin D intake habits and physical activity levels of the assessed men and women.

The connection between BMI levels and vitamin D status among 50-80 years old female population in South-Hungary

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Objective: Nowadays, obesity has become a global health problem and the number of obese people is continuously increasing. The health status of obese people is worse than those with normal weight. Obesity is a risk factor of several deseases, for example cardiovascular and musculosceletal deseases, psychiatric problems. The level of vitamin D is decreasing with age, due to the non appropriate nutritional intake and the skin's decreased ability to synthetise it. Low vitamin D increases the risk of chronic widespread pain and if obesity is present than the health status severely deteriorates. The aim of this study was to examine the connection between Body Mass Index (BMI) and vitamin D among women aged 50-80 years.

Design and methods: We examined 219 women from South-Hungary within the OTKA NN110932 study. We measured body weight and height and from the results calculated BMI. We also took blood samples to specify vitamin D level. The datas were inserted into an electronic database with a software designed for the study. The statistical analysis was calculated with SPSS 24 program. During the analysis we used descriptive and correlation statistics and analysis of variance.

Results: The mean BMI value for all women is 29,4 kg/m^2 and the mean value of vitamin D level is 67,7 nmol/L. BMI increases with age. The vitamin D level is the highest at the 60-69 age group. We found a significant, inverse correlation between BMI and vitamin D looking at all participants. Adjusting for age groups, there is a significat, inverse relationship only at the 50-59 age group.

Conclusion: Our results do not match with the reviewed literature. In the assessed population the significant relationship between BMI and vitamin D levels disappeares after adjusting for age. The intake of vitamin D is inapproriate and the participants have higher BMI than normal level.