

## **CURRICULUM VITAE**

### **MICHAIL N. VARRAS**

#### **Summary CV:**

Mr Michail Varras received his Medical Degree (M.D.) from the Medical School of Aristoteleion University of Thessaloniki, Greece. He underwent a residency in General Surgery (one year) and in Obstetrics and Gynecology at the First Department of Obstetrics and Gynecology, Kapodistreiakon University of Athens, "Alexandra" General Hospital, Athens, Greece (four years). He is married and has two daughters studying Pharmacy. He holds three postgraduate qualifications (MSc) in "Health Management" (Department of Economics, University of Piraeus, Greece), in "Reproductive-Regenerative Medicine" (First Department of Obstetrics and Gynaecology, Medical School, National Kapodistreiakon University of Athens, Greece) and in "Minimally Invasive Surgery, Robotic Surgery and Telesurgery" (Department of Surgery, Medical School, National Kapodistreiakon University of Athens, Greece). He holds a Ph.D. in Molecular Gynecological Oncology, National Hellenic Research Foundation and Laboratory of Clinical Virology, School of Medicine, University of Crete, Greece. He has been trained in "Reproductive Biology" at the Centre for Reproductive Medicine, Department of Obstetrics and Gynaecology, University of Edinburgh, UK, in "Gynaecological Laparoscopic Surgery and Hysteroscopy" at the Royal Free Hospital, London, UK (scholarship from the "Lillian Voudouris" Foundation), in "Assisted Reproduction", Hammersmith Hospital, London (scholarship from the "Lillian Voudouris" Foundation), in "Fetal Medicine" at the Harris Birthright Center of Fetal Medicine, King's College Hospital, London, UK (approved by the Greek Central Board of Health) and in "Reproductive Medicine" at the St Bartholomew's Hospital, London, UK (approved by the Greek Central Board of Health). He has also been trained in the use of ultrasounds in Obstetrics - Gynaecology and in Fetomaternal Medicine at the "Elena Venizelou" General State Hospital of Athens, Greece. He has been trained in specific areas of Health Management such as "Quality Assurance in the "Provision of Health Services" (Vocational Training Center, Athens General Hospital "Hippocrates" and Napier University Edinburgh Scotland) and "Policies for the Development and Promotion of Public Health" at National and International Level" (National School of Public Health and World Health Organization, WHO Regional Office in Europe). He has been practicing medicine as a qualified Obstetrician-Gynaecologist since January 2000 getting adequate experiences, documented by his work at many Tertiary State Hospitals of Greece such as "George Chatzikosta", General Hospital of Ioannina, Ioannina, "George Gennimatas", General Hospital of Athens, Athens, "ATTIKON", General Hospital of Athens, Athens, "St Savvas", Oncologic Hospital of Athens, Athens. Currently he is working as a specialist Consultant in Obstetrics and Gynaecology at "Elena Venizelou" General Maternity State Hospital of Athens, Athens, Greece. He has independent teaching experiences as academic fellow at the

Technological Institute of Athens and the University of the Peloponnese and as Assistant Professor at the University of Patras. He has significant scientific activity with contribution of numerous publications in scientifically acclaimed International and Greek medical journals and books. He has also participated as a speaker at a significant number of International and Greek medical conferences presenting his scientific work. He has been awarded twice by the Greek Society of Obstetrics and Gynaecology, a member of FIGO for his contribution to Obstetrics and Gynaecology. He is serving as a reviewer for several peer-reviewed journals.

### Education:

- 1981: After a nationwide entrance examination registration and studying the first year of the **Civil Engineering Section**, Aristoteleion University of Thessaloniki, Thessaloniki, Greece
- 1982-1989: **Medical School**, Aristotelion University, Thessaloniki, Greece, **Ptychio Iatrikes**, 19/4/1989 Degree at grade eight from a possible maximum of ten (**very good**)
- **October 1993 – February 1994: First part** (formal taught component) of the **MSc/Diploma Course in Reproductive Biology**, offered by the Department of Obstetrics and Gynecology, University of Edinburgh, Scotland, U.K. **Faculty:** Prof. DW Lincoln, Prof. AS McNeilly, Prof. S. Hillier, Prof. A. Calder, Prof. D.T. Baird., Dr. T. Bramley, Dr. N. Brooks, Dr R.M. Sharpe, Dr. J.D. West, Dr. G. Lincolson, Dr. J.A.. Russel, Dr. H. Critchley, Dr. F. Johnstone, Dr. R. Kelly

**Exercise in:** ovulation induction protocols, protocols investigating amenorrhea, gonadal physiology testicles, ovaries gonadal physiology, reproductive biochemistry, embryology and genetics, regulation of fertility and contraception, material culture in assisted reproduction techniques of cultivation of embryos to the blastocyst stage, cooling techniques embryos, preparation of sperm and eggs for assisted reproduction, radiation protection and safety with radioisotopes, animal handling, statistics and computers, techniques of hormones with radio-immunoassays (radioimmunoassay, RIA), techniques of molecular genetics in preimplantation diagnosis of genetic disorders, pituitary immunocytochemistry, cultured granulosa cells of the ovary, pharmacological manipulation of uterine contractions, sexual behavior and scientific methodology and ethics.

### Training in the following topics:

Reproductive Biochemistry, Hypothalamic-Pituitary Regulation, Testicular Gonadal Physiology, Ovarian Gonadal Physiology, Pregnancy and Childbirth, Gametal Biology, Embryology and Genetics, Regulation of Fertility and Contraception, Infertility and Assisted Reproduction, Sexual Behaviour, Scientific Methodology and Ethics, Radiation Protection and Safety with

Radioisotopes, Manipulation of Animal models, Statistic and Computers, Receptor Binding to its Hormone and Scatchard Analysis, Pituitral Immunocytochemistry, In situ Hybridism (centromere of chromosome 1), Culture of Ovarian Granulosa Cells and Radioimmunoassay of Estroges, Pharmacological Handling of Uterine Contractions, Microdissection of Testicula Tubules, Electrophoresis in Polyacrylamide Gel, Western Blot analysis of *c-myc* in Corpus Luteum.

- **1994- 1997:** Research for **Ph.D. Degree** in Basic Sciences, Laboratory of Clinical Virology, Medical School, University of Crete, Heraklion, Greece and Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, Athens, Greece.  
**Ph.D. Degree**, 18/12/1997 at **Grade excellent**.  
**Title of Ph.D. thesis:** “**Detection of *ras* gene mutations using PCR technology in ovarian tumours and endometrial carcinoma and interaction of the *H-ras* with tumor suppressor protein P53 in ovarian tumors and endometrial carcinomas**”.
- Post-graduate training in “**Health Management**” (Part-Time) and acquisition of **Master of Science (M.Sc.) Degree in “Health Management”**, University of Pireaus, Attiki, Greece, at **Grade excellent**, 09/20/2007.

Study for four semesters in theoretical and practical training and examinations at the end of each semester in the following topics:

#### A' semester

**Introduction in Economics** (grade 9 out of 10)

**Accountancy** (grade 8 out of 10)

**Mathematics for Economics** (grade 8 out 10)

**Statistic** (grade 7 out of 10)

#### B' semester

**Marketing and Health** (grade 9 out of 10)

**Management of Human Resources** (grade 10 out of 10)

**Economic Analysis** (grade 8 out of 10)

**Amount Analysis** (grade 10 out of 10)

#### C' semester

**Health Economics** (grade 9 out of 10)

**Insurance systems and Organization** (grade 8 out of 10)

**Valuation of Investment in Health Programs** (grade 8 out of 10)

**Health Politics in Greece and European Community** (grade 8 out of 10)

#### D' semester

**Health Organize and Management** (10 out of 10)

**Management of Human Resources** (10 out of 10)

**Formatic Systems** (9.10 out to 10)

**Thesis for Master Degree** (7.50 out of 10)

**Title of Thesis for Master Degree in “Health Management”: “Business plan for the constitution and development of a private nursing home”.**

- Post-graduate training in **“Reproductive-Regenerative Medicine” (Part-Time)** and acquisition of **Master of Science (M.Sc.) Degree in “Reproductive-Regenerative Medicine”**, Medical School, University of Athens, Attiki, Greece, at **Grade very good, 03/02/2011.**

Study for two semesters in theoretical and practical training and examinations at the end of each semester in the following topics:

**A' semester**

- **Application of P/C and statistics in modern research** (grade 8 out of 10)
- **Molecular Biology of Reproduction** (grade 7 out of 10)
- **Anatomy and Physiology of Reproductive Tract** (grade 8 out of 10)
- **Gametogenesis and Preimplantation genetic diagnosis** (grade 8 out of 10)
- **Endocrinology of Pregnancy - Fetal Development** (grade 7 out of 10)
- **Pathophysiology of Reproductive Tract** (grade 8 out of 10)

**B' semester**

- **Infertility and Assisted Reproduction** (grade 7 out of 10)
- **Methodology of IVF** (grade 8 out of 10)
- **Reproductive Endocrinology** (grade 6 out of 10)
- **Prenatal Testing and Diagnosis** (grade 7 out of 10)
- **Regenerative Medicine** (grade 7 out of 10)
- **Current Developments in Reproductive Medicine** (grade 7 out of 10)

Object and purpose of the graduate program was to provide a high level of expertise and training in research in Reproductive Medicine.

The Reproductive Medicine is a field that is constantly evolving and deals with the physiology, pathology and endocrinology of the reproductive tract in women and men, as well as genetic disorders and interfere both conservative and surgical treatment to them. Also has an important contribution to couples facing infertility problems. Existing techniques (IVF, ICSI, MESA, TESA), combined with preimplantation genetic diagnosis (PGD), have resulted in millions of births of healthy children, and new techniques are being tested (in vitro oocytes maturation-IVM, IVG), believed that in the future will solve problems that might arise from the application of the existing techniques.

Regenerative medicine is a new field of medical research that deals with the study of stem cells and applying the results of this research into clinical practice, with the aim of therapeutic intervention in a significant number of patients.

**Title of Thesis for Master Degree in “Reproductive-Regenerative Medicine”: “Study of the expression levels of Oct-4, survivin and DAZL genes from human follicular luteinized granulosa cells from women**

**undergoing in vitro fertilization (IVF) or microfertilization (ICSI) - embryo transfer: Clinical Correlations”.**

- Post-graduate training in **“Minimally Invasive Surgery, Robotic Surgery and Telesurgery”**, Medical School, University of Athens, Attiki, Greece **(Part-Time)** and acquisition of **Master of Science (M.Sc.) Degree in “Minimally Invasive Surgery, Robotic Surgery and Telesurgery”**, **16/07/2015** at **Grade very good (8.10)**.

Study for four semesters in theoretical and practical training and examinations at the end of each semester in the following topics:

**A' semester:**

- **(A-1) Research Ethics of Medicine** (grade 10 out of 10)
- **(A-2) Minimally Invasive Surgery: Operation and Use of Related Equipments** (grade 9 out of 10)
- **(A-3) Medical Informatics** (grade 8 out of 10)
- **(A-4) Biology of tumors and surgery** (grade 9 out of 10)
- **(A-5) Basic Surgical Research and Experimental Surgery** (grade 8.5 out of 10)
- **(A-6) Endoscopic Surgical Anatomy** (grade 9 out of 10)
- **(A-7) Biochemical and Biological Effects of Minimally Invasive Techniques** (grade 5 out of 10).
- **(A-8) Blood Disorders and Minimally Invasive Techniques** (grade 8 out of 10)
- **(A-9) Minimally Invasive Techniques and Oncology** (grade 7.5 out of 10)
- **(A-10) Anesthesia and Minimally Invasive Techniques** (grade 10 out of 10)

**B' semester:**

- **(B-1) Minimally Invasive Techniques in Biliary Surgery** (grade 7 out of 10)
- **(B-2) Minimally Invasive Surgery of the Upper Digestive System and Bariatric Surgery** (grade 7 out of 10)
- **(B-3) Minimally Invasive Techniques in Colon Surgery** (grade 5 out of 10)
- **(B-4) Minimally Invasive Techniques for the Surgery of Solid Organs** (grade 6 out of 10)
- **(B-5) Minimally Invasive Surgery of Abdominal Wall Hernias** (grade 6 out of 10)
- **(B-6) Invasive Endoscopic Techniques in Gastrointestinal System** (grade 6 out of 10)
- **(B-7) Minimally Invasive Techniques in Endocrine Surgery** (grade 6 out of 10)
- **(B-8) Minimally Invasive Thoracoscopic Techniques** (grade 6 out of 10)

- **(B-9) Minimally Invasive and Endoscopic Techniques in Gynecology** (grade 10 out of 10)
- **(B-10) Minimally Invasive Techniques in Urology** (grade 8 out of 10)
- **(B-11) Minimally Invasive Techniques in Otolaryngology** (grade 9 out of 10)
- **(B-12) Minimally Invasive Techniques in Vascular Surgery** (grade 8 out of 10)
- **(B-13) Minimally Invasive Techniques in Organ Transplantations** (grade 6 out of 10)
- **(B-14) Biomedical Engineering** (grade 8 out of 10)
- **(B-15) Principles in Telesurgery and Robotic Surgery** (grade 7 out of 10)

**C' semester:**

- **(C-1) Application of Laparoendoscopic techniques in simulators** (grade 9 out of 10)
- **(C-2) Experimental Billiary Surgery** (grade 7 out of 10)
- **(C-3) Experimental Colon Surgery** (grade 5 out of 10)
- **(C-4) Experimental Surgery of Solid Organs** (grade 6 out of 10)
- **(C5) Experimental Surgery of Abdominal Wall Hernias** (grade 6 out of 10)
- **(C-6) Experimental Endocrine Surgery** (grade 6 out of 10)
- **(C-7) Experimental Surgery in Urology** (grade 8 out of 10)
- **(C-8) Experimental Surgery in Organ Transplantations** (grade 6 out of 10)

**D' semester – Research Thesis**

**Title of Thesis for Master Degree in “Reproductive-Regenerative Medicine”:** “Assessment of laparoscopic surgical skills acquired on laparoscopic virtual reality simulator compared to box trainer: an analysis of obstetrics-gynecology residents”.

- **Practice in Obstetrics-Gynaecology (i).** General Hospital of Trikala, Trikala, Greece from 08/05/1991 to 04/08/1992, practice in general surgery, 1 year. **(ii).** General Hospital "Alexandra", First Department of Obstetrics - Gynecology, University of Athens, Athens, from 08.03.1994 to 08.03.1998, practice in Obstetrics and Gynecology, 4 years. Acquisition of title in medical specialty: “**Obstetrics and Gynecology**”, 26/05/1998, Athens Prefecture, Greece.
- **General Medical Council of UK:** Number of registration: 4455154, Obstetrics and Gynaecology 8 Sept 1998

**English Courses Attended:**

**General English Language Courses:**

- Stradbrook College, Sheffield: full time - **ten weeks**

- Anglia University, Cambridge: full time - **ten weeks**
- The Bell School, Cambridge: full time - **ten weeks**

**English for Medical Studies and Practice** - Institute of Applied Language, University of Edinburgh: full time - 20 hours per week during the period from 5 of July to 23 of July 1993 & from 26 of July to 13 of Αυγούστου 1993 & from 16 of July to 3 of September 1993 & from 6 of July to 24 of September 1993 (**total 240 hours**)

**First Certificate in English**, University of Cambridge, Local Examinations, Syndicate International Examinations, June 1995, Athens Ref Number 956GR0050249

### **Practice in Medicine:**

- **Military Service as a Rifleman Physician** from May 1989 to November 1990. Swearing as a Reserve Military Officer of the Greek Army, 31/03/2000, Ioannina, Greece

- **General Practitioner – Rural Duty:**

**Community Clinic of Antikithira Island, Greece** from 25.06.90 to 09.11.90

**Community Clinic of Platanos Village, Trikala, Greece** from 07.12.90 to 25.07.91 - Parallel responsibilities as the physician of Health Department, Prefecture of Trikala, Trikala, from 18-03-1991 to 25/07/1991.

- **Department of General Surgery, General State Hospital, Trikala, Greece**

Registrar in General Surgery from 05.08.91 to 04.08.92 for completion of one year in General Surgery in order to obtain the title of Specialist in Obstetrics and Gynaecology

- **1st Department of Obstetrics & Gynaecology, University of Athens, 'Alexandra' Hospital, Athens, Greece**

Registrar for Specialisation in Obstetrics and Gynaecology from 08.03.94 to 08.03.98

- **Minimally Invasive Therapy Unit and Endoscopy Training Centre, University Department of Obstetrics and Gynaecology, The Royal Free Hospital, London, U.K.**

Clinical Research Fellow in Gynaecological Endoscopic Surgery from 7/9/98 to 30/10/1999. **Scholarship from “Lilian Voudouri” Foundation, Athens, Greece** for 12 months training in Gynaecological Endoscopic Surgery – Practice in Diagnostic Hysteroscopy and Hysteroscopic Biopsies, Hysteroscopic Endometrial Polyps Removal, Hysteroscopic Endometrial Adhesiolysis, Hysteroscopic Transcervical Endometrial Resection, Diagnostic Laparoscopy, Laparoscopic Salpingectomy, Laparoscopic Salpingotomy for the treatment of ectopic pregnancy, Laparoscopic Treatment of PCOS Syndrome with Diathermy, Laparoscopic Salpingo-oophorectomy, Laparoscopic Ovarian Cystectomy, Laparoscopic Treatment of Endometriosis, Laparoscopic Adhesiolysis, Laparoscopically Assisted Vaginal Hysterectomy and Vaginal Hysterectomy.

- **“IVF Unit”, Division of Paediatrics, Obstetrics and Gynaecology, Hammersmith Hospital, London, U.K.**

Clinical Research Fellow in IVF from 01/10/1999 to 10/12/1999. **Scholarship from “Lilian Voudouri” Foundation, Athens, Greece** for training in IVF – Training in Investigation of Infertile Couple, Gynecological Ultrasound in the IVF Unit, Ovulation Induction Protocols, Oocyte Retrieval, Embryotransfer and Intrauterine Insemination.

- **“G. Chatzikosta” General State Hospital, Ioannina, Greece. Department of Obstetrics and Gynaecology.**

Consultant in Obstetrics and Gynaecology from 17/01/2000 to 31/05/2000.

- **“G. Gennimatas” General State Hospital, Athens, Greece. Department of Gynaecology.**

Consultant in Obstetrics and Gynaecology from 01/06/2000 to 12/06/2002.

- **“Attikon”, University General Hospital, Athens, Greece. Department of Obstetrics and Gynaecology.**

Consultant in Obstetrics and Gynaecology from 12/06/2002 to 08/09/2004.

- **Anticancer Oncologic Hospital of Athens “AGIOS SAVVAS”, Athens, Greece. Department of Gynaecology.**

Consultant in Gynaecology from 09/09/2004 to 05/12/2004.

- **“Tzaneio” General State Hospital, Piraeus, Attiki, Greece-Departement of Obstetrics and Gynaecology.**

Consultant in Gynaecology from 06/12/2004 to 31/03/2010 (5 έτη & 3 μήνες) - Attachment for six months in fetal medicine at the Harris Birthright Center of **Fetal Medicine** του King’s College Hospital NHS Foundation Trust of London, U.K. under the supervision of Prof. K. Nikolaides (from 03/11/2008 to 21/05/2009) – Approval from the Central Board of Health, Greek Ministry of Health and Social Solidarity, Athens, Greece. Observation of the activities of the Fetal Medicine Department with included: ultrasound screening for chromosomal abnormalities at 11-13<sup>+6</sup> weeks of pregnancy with fetal NT and assessment of the presence or absence of the nasal bone, obstetrics ultrasounds for prenatal diagnosis of congenital abnormalities such as hydrocephalus, spina bifida, abnormalities of the face (cleft lip, palate), lung tumors, kidney and gastrointestinal disorders, skeletal dysplasias and indicators for chromosomal abnormalities, sonographic assessment of the length of the cervical length for predicting preterm labor, fetal echocardiography, ultrasound Doppler measurement of uterine arteries, fetal middle cerebral artery and the ductus venosus for assessing placental function and fetal circulation, CVS and amniocentesis for fetal karyotyping and prenatal diagnosis of genetic disorders by DNA analysis, omphalocentesis for fetal

blood transfusion or platelets in alloimmune thrombocytopenia, endoscopic laser ablation for severe twin-to-twin transfusion and endoscopic intratracheal positioning balloon in fetuses with diaphragmatic hernia.

- **“Elena Venizelou”, General Maternity Hospital, Athens, Greece. Third Department of Obstetrics and Gynaecology.**

Consultant in Obstetrics and Gynaecology from 01/04/2010 to 14/06/2016 – Special Training in **Obstetrical and Gynecological Ultrasounds and Fetal-Maternal Medicine**, three times per week at the same Hospital (6<sup>th</sup> Department of Obstetrics and Gynecology) for 18 months duration from **26/4/2012 to 25/10/2013. Director in Obstetrics and Gynaecology** from 15-06-2016 to today.

Licence for **Obstetrics and Gynaecology Ultrasound Scans** from the **Greek Ministry of Health**.

### **PC use knowledge and typing ability**

### **Teaching Experiences:**

- Participation in teaching and educating medical doctors in Workshops (working group) about the indications, application security, technical limitations of minimally invasive techniques and practice in endoscopic methods in the field of gynecologic laparoscopy and hysteroscopy: **“Hand On” Gynecological Endoscopy Workshop**, Minimally Invasive Therapy Unit & Endoscopy Training Centre, University Department of Obstetrics and Gynecology, Royal Free Hospital, London, U.K., 16-18 Σεπτεμβρίου 1998 & 18-20 Νοεμβρίου 1998 & 3 Δεκεμβρίου 1998 & 20-22 Ιανουαρίου 1999 & 10-12 Μαρτίου 1999 & 22 Απριλίου 1999 & 12-14 Μαΐου 1999 & 10 Ιουνίου 1999 & 7-9 Ιουλίου 1999.
- Participation in surgical teaching and training of **junior doctors in “Obstetrics - Gynecology”**: Providing a modern and valuable clinical training of junior doctors in the subject of “Obstetrics – Gynecology” and courses analysing specific case studies, bibliographic information and lectures from 2000 to today as a Consultant in Obstetrics and Gynaecology of the Greek National Health System.
- Participation in teaching and training of other health professions other than physicians and dentists: **(i). Gynaecological Endoscopy Course for Nurses**, 25 of February 1999, «Minimally Invasive Therapy Unit & Endoscopy Training Centre, University Department of Obstetrics and Gynaecology, Royal Free Hospital, London, UK **(ii)**. Teaching as a **Research Associate in Obstetrics and Gynecology** of the Midwifery Department, Higher Technological University of Athens, Athens, Greece during the fall semester of the student year 1999-2000 (3 hours per week) **(iii)**. Teaching as a Research Associate in Obstetrics and Gynecology of the “Health Visitors” Department, Higher Technological

University of Athens, Athens, Greece during the fall semester of the student year 1999-2000 (2 hours per week) (iv). Participation as an **Instructor** at Vocational Training Institution of Athens, Athens, Greece, Greek Ministry of Health and Social Solidarity for specialty in **"Paramedic - Ambulance Crew"** teaching the course **"Urgent problems in Obstetrics - Gynecology"** 5 hours on 11/03/2002 & 5 hours on 22/03/2002.

- Participation in training medical doctors in approved by the Greek Ministry of Health and Social Solidarity, Athens, Greece action **"The Use of Ultrasounds in Obstetrics – Gynecology"**, total duration 80 hours. The program was implemented by the Center for Professional Training, "Ippokrapeion" Hospital of Athens, Greece from 06/09/2004 to 22/10/2004 - addressed to Medical Staff as an instructor in theoretical training with four (4) hours and in practice with forty two (42) credit hours.

**Ability to mentor and promote research including significant contributions in research projects:**

Join the period from 19/05/1994 to 31/08/1998 actively and effectively in research programs (Molecular Oncology) funded by the **Laboratory of Clinical Virology, Department of Medicine, University of Crete and the Laboratory of Molecular Oncology and Biotechnology, National Hellenic Research Foundation :**

- **Detection of *ras* gene mutations by the technique of PCR in tumors of the ovary and endometrial cancer and interaction of the tumor suppressor proteint P53 with H-*ras* (Doctorate Thesis).**
- **Regulation of proto-oncogene H-*ras* by the receptors of steroid-hormones**
- **Detection of human papillomavirus (HPV) and K-*ras* mutations by the PCR technique in cytological materials from cervical carcinomas.**
- **Detection of *ras* oncogenes mutations in cancer cells from ascitic fluid or peritoneal aspiration in ovarian cancer.**

Introduction of Research and actively participate in research with the topic **"Determination of the value of intraperitoneal local anesthesia administration with bupivacaine in reducing postoperative pain and analgesic needs of women after gynecologic operative laparoscopy"** in Minimally Invasive Therapy Unit & Endoscopy Training Centre, University Department of Obstetrics and Gynaecology, Royal Free Hospital, London, UK

Introduction of Research and actively participate in research with the topic **"Determination of the genes expression Oct-4, survivin and DAZL from**

**human follicular luteinized granulosa cells from women undergoing in vitro fertilization - embryo transfer: Clinical Correlations." (Thesis, for M.Sc. in "Reproductive - Regenerative Medicine", Medical School, University of Athens, Greece)**

Introduction of Research and actively participate in research with the topic **"Assessment of laparoscopic surgical skills acquired on laparoscopic virtual reality simulator compared to box trainer: an analysis of obstetrics-gynecology residents"** (Thesis, for M.Sc. in **"Minimally Invasive Surgery – Robotic Surgery and Telesurgery"**, Medical School, University of Athens, Greece).

#### **Participation in ongoing training activities as a trainee:**

- **"Methods of Laparoscopic Suturing"**: Total duration 60 hours with 24 hours of theoretical and 36 hours of practical training. The program was implemented from 11/09/2000 to 30/09/2000 under the Operational Program 940005 E1 **"Health–Providence"**, Second Community Support Framework, The Vocational Training Centre "Evangelismos" General Hospital, co-financed by the European Social Fund and the Greek Ministry of Health and Social Solidarity.
- **"Ensuring quality health services"**, 150 hours total duration of training at the Vocational Training Centre, "Ippokrateion" General Hospital of Athens, Greece, code Y02Y.07-YE/EDS702 and combination of education at the Napier University of Edinburgh, Scotland (UK). Date of completion of training 15/10/2003.
- **"Policies for the Development and Promotion of Public Health at National and International Level"** from 04/09/2006 to 06/10/2006, a total duration of 150 hours (104 hours of theoretical training and 46 hours training). The program was implemented at the The Vocational Training Centre of the National School of Public Health, Athens, Greece with 3A7 energy training code. Also, the course had a tough part at the World Health Organization (Copenhagen, Denmark): **"Public Health Policy and Systems in the European Region"**, **World Health Organisation, Copenhagen, Denmark** (WHO Regional Office in Europe) from 02 to 06 October 2006.

**Member of "Athens Medical Associations", Athens, Greece**

**Member of the "Greek Society of Obstetrics and Gynecology"**

**Participation in Marquis WHO'S WHO in the World** from 2007 to today, for my silent contribution to the medical science.

- **Editor-in-Chief of the International Journal "OA Case Reports"**  
<http://www.oapublishinglondon.com/oa-case-reports> (From December 2012 to December 2015).

- **Member of the EDITORIAL BOARD in the International Medical Journal “Clinical and Experimental Obstetrics and Gynecology” (ISSN: 0390-6663).** The Journal publishes original work, preferably brief reports, in the fields of Gynaecology, Obstetrics, Foetal Medicine, Gynaecological Endocrinology and related subjects: Fertility and Sterility, Menopause, Urogynaecology, Ultrasound in Obstetrics and Gynaecology, Sexually Transmitted Diseases. The Journal is covered by INDEX MEDICUS, MEDLINE, EMBASE/Excerpta Medica, BIOSIS.  
**Issues as a member of the Editorial Board:** 2003, 30 (4) - 2004, 31 (1) - 2004, 31 (2) - 2004, 31 (3) - 2004, 31 (4) - 2005, 32 (1) - 2005, 32 (2) - 2005, 32 (3) - 2005, 32 (4) - 2006, 33 (1) - 2006, 33 (2) - 2006, 33 (3) - 2006, 33 (4) - 2007, 34 (1) - 2007, 34 (2) - 2007, 34 (3) - 2007, 34 (4) - 2008, 35 (1) - 2008, 35 (2) - 2008, 35 (3) - 2008, 35 (4) - 2009, 36 (1) - 2009, 36 (2) - 2009, 36 (3) - 2009, 36 (4) - 2009, 37 (1) - 2010, 37 (2) - 2010, 37 (3) - 2010, 37 (4) - 2010, 38 (1) - 2011, 38 (2) - 2011, 38 (3) - 2011, 38 (4) - 2011, 39 (1) - 2012, 39 (2) - 2012, 39 (3) - 2012, 39 (4) - 2012, 40 (1) - 2013, 40 (2) - 2013 to today.
- **Member of the EDITORIAL BOARD in the International Medical Journal “Case Reports in Medicine”, Hindawi Publishing Corporation (ISSN: 1687-9627, e-ISSN: 1687-9635).** The articles of Case Reports in Medicine are indexed/reviewed in the following databases/resources: Academic Search Complete, Biological Sciences, BioMedSearch.com, Calcium and Calcified Tissue Abstracts, CINAHL: Cumulative Index to Nursing and Allied Health Literature, CSA Illustrata - Natural Sciences, CSA Neurosciences Abstracts, Current Abstracts, Directory of Open Access Journals (DOAJ), Google Scholar, Open J-Gate, PubMed, PubMed Central
- **Reviewer of medical manuscripts**

  - “Human Reproduction”
  - “Gynecology and Obstetrics Investigation”
  - “Gynecological Endocrinology”
  - “Maturitas”
  - “European Journal of Obstetrics and Gynecology and Reproductive Biology”
  - “World Journal of Surgical Oncology”
  - “Archives in Gynecology and Obstetrics”
  - “Indian Journal of Cancer”
  - “Journal of Obstetrics and Gynecology Research”
  - “Journal of Medical Case Reports”
  - “European Journal of Surgical Oncology”
  - “Journal of Human Reproductive Sciences”
  - “SRX Medicine Journal”
  - “Clinical Medicine: Case Reports”
  - “Clinical Medicine: Women's Health”
  - “Clinical Medicine: Reproductive Health”
  - “Oman Medical Journal”
  - “Rare Tumors”

- “Reproductive Biology Insights”
- “Nigerian Journal of Clinical Practice”
- “Journal of Pancreas”
- “Annals of Medical and Health Sciences Research”
- “Medical Science Monitoring”
- International Journal of Surgery Case Reports
- JOURNAL OF ASSISTED REPRODUCTION AND GENETICS
- Journal of Women's Health Care
- Open Journal of Obstetrics and Gynecology
- SURGICAL SCIENCE

**The research interests are focused in the following fields:**

- **Molecular Oncology – Histology:** Molecular analysis and study of genetic changes in benign and malignant tumors of the female genital tract and their correlation with clinical and pathological parameters of patients.
- **Physiology of Reproduction – Embryology:** Molecular analysis and study of genetic changes in granulosa cells of ovarian follicles in women undergoing assisted reproduction and embryo transfer and correlation of the genetic changes and clinical parameters.
- **Physiology of Reproduction – Embryology:** Effect of system insulin like growth factor in placentas of normal and pathological pregnancies and interaction with clinical parameters.
- **Physiology of Reproduction – Embryology:** Study of local estrogen administration in the treatment of atrophic vaginitis in postmenopausal women.
- **Laparoscopic Surgery:** Study of the value of long-term local anesthetics in reducing postoperative pain in gynecological laparoscopy.
- **Gynaecological and Obstetrics Ultrasonography:** Study of pathological conditions of the genital tract of women using ultrasound such as congenital anomalies, adnexal torsions, salpingo-ovarian abscesses and correlation of these pathological situations with haematological and biochemical diagnostic tests and pathological findings. Fetal developmental malformations and literature analysis.
- **Rare Conditions in Obstetrics and Gynecology:** Research and study of very rare clinical cases (case studies) in Obstetrics and Gynaecology with analysis of the literature.

- **Anatomy:** Ultrasonographic and Surgical – Laparoscopic Anatomy – Molecular Anatomy.
- **Surgical Simulation for Medical Education and Practice in Minimally Invasive Surgery and Anatomy:** Research and study in the laparoscopic surgical skills obtained from medical students, residents in surgical specialties and specialized fellows after the training in laparoscopic simulators and trainer boxes.

## AWARDS

- From the **Greek Society of Obstetrics and Gynecology**, Member of the FIGO, the physician **Dr Michail Varras** and partners were awarded on 26 of November 1994 with the Honorary Diploma Award **in memory of "Ioannis Mantalenakis"** and 300,000 greek drachmas prize money for the best free communication to the **6th National Congress of Obstetrics and Gynecology, Athens, Greece** entitled **"Activation of the oncogene K-ras in tumors of the endometrium"**.
- From the **Greek Society of Obstetrics and Gynecology**, Member of the FIGO, the physician **Dr Michail Varras** and partners were awarded on 20 of May 2012 under the **12th National Congress of Obstetrics - Gynecology, 17-20 May 2012, Thessaloniki, Greece** with the Award and 500 euros prize money for the best free communication of the conference entitled **"Study of the expression levels of genes Oct-4, DAZL, and survivin in human follicular luteinized granulosa cells of the ovaries, in women undergoing ovulation induction for *in vitro* fertilization (IVF) or ICSI (ICSI) and embryo transfer: clinical correlations"**.

## KNOWLEDGE OF LANGUAGES:

**MOTHER TONGUE:** Greek

**OTHER LANGUAGES:** English

## LIST OF PUBLICATIONS

### Scientific Projects

## A. Ph.D. Thesis

**PhD thesis** entitled “**Determination of *ras* oncogenes mutations with the technique of PCR in ovarian tumors and endometrial carcinomas and interaction of P53 tumor suppressor protein with H-*ras*”**, **Michail Varras**.

**Body responsible:** Department of Medicine, University of Crete, Heraklion, Laboratory of Molecular Oncology and Biotechnology, Institute of Biological Research and Biotechnology and National Hellenic Research Foundation, Athens.

Receive of Doctorate Degree (Diploma Thesis for Doctorate) with grade "excellent" on 18/12/1997 and swearing on 23/12/1997.

### **Abstract:**

The *ras* family of cellular oncogenes is implicated in a variety of human neoplasias. Point mutations of the *ras* oncogene constitute of basic mechanism of human carcinogenesis and the frequency depends on the type of neoplasms or the ethnic groups. In this study, using PCR-RFLP analysis we detected activated *ras* genes, in human endometrial carcinomas and ovarian tumors of Greek patients. Concerning human primary endometrial carcinomas, *K-ras* gene point mutations were detected in 15% of cases, *H-ras* in 7.3%, while no mutations were found for the *N-ras* gene. Concerning human primary ovarian carcinomas, the prevalence of mutations in *K-ras* gene was 1/8 (13%) in mucinous, 7/29 (24%) in serous, 1/3 (33%) in endometrioid and 2/8 (25%) in clear cell adenocarcinomas, and in *H-ras* gene 1/8 (13%) in mucinous and in 2/99 (7.4%) in serous adenocarcinomas. These results show the role of *ras* gene mutations in the development of human endometrial and ovarian carcinomas in Greek population. In addition, the statistic analysis of the results suggests that *H-ras* activation by codon 12 point mutations may be a late event in the progression of endometrial carcinomas. The P53 tumor-suppressor protein prevents genetic alterations due to genotoxic stress (chemical or radiation). P53 also regulate gene expression, e.g. *H-ras*. Using nuclear extracts from human primary endometrial and ovarian carcinomas and from adjacent normal tissue in gel retardation assays, we tested the binding levels of the P53 protein to the *H-ras* p53 element in tumor versus normal tissue. Concerning endometrial carcinomas, elevated P53 binding in the tumor tissue was found in 5/11 (45%) pairs tested, thus suggesting overexpression of the wild-type P53, or P53 mutated forms that bind DNA. In 3/11 (27%) pairs tested, there was no difference in the level of P53 binding, thus suggesting no difference in the levels of P53 binding, thus suggesting no alteration in the P53 locus. In 3/11 (27%) cases, no P53 binding was detected, indicating P53 mutated forms that fail to bind DNA. Concerning ovarian carcinomas, elevated P53 binding in the tumor tissue was found in 2/5 (40%) pairs tested, no difference in P53 binding levels in 2/5 (40%) and no P53 binding in tumor tissue in 1/5 (20%) of cases. These experimental results suggest a direct implication of the *H-ras* gene in the development of endometrial and ovarian carcinomas, through abnormal regulation of the P53 protein.

## B. Thesis for Master Degree of Science in “HEALTH MANAGEMENT”

**“Business plan for the constitution and development of a private nursing home”:**

**Michail Varras.**

**Body responsible:** University of Piraeus, Attica, Greece (Section of economic science). Number of pages: 104.

**Abstract:**

The constitution and development of a hypothetical case of a private nursing home are studied regarding the collection and analysis of empiric data for the market, the cost of construction of the building, the cost of the accoutrements, the working cost, the incoming and the management of the unit. The purpose of the company is the nursing of the overage people protist with chronic medical problems such as kinetic disabilities and sinility. The study estimates the investment studying the payback period, the net present value, the rate of benefit – cost and makes the break even analysis.

**C. Thesis for Master Degree of Science in “REPRODUCTIVE AND REGENERATIVE MEDICINE”**

**“Study of expression levels of Oct-4, DAZL and survivin genes in human luteinized granulosa cells of women undergoing ovulation induction for IVF or ICSI end embrio transfer: clinical correlations”, Michail Varras.**

**Body responsible:** National Kapodistrian University of Athens, Faculty of Health Sciences, Medical School.

Number of pages: 258.

**Abstract:**

**Objective:** To determine the incidence of expression of SURVIVIN, OCT-4 and DAZL in human granulosa cells during ovarian stimulation in women with normal FSH levels, undergoning IVF or ICSI. To investigate the presence or not of stem cells in follicular granulosa cells. To test if the levels of genes expression in granulosa cells could indicate number of oocytes retrieved, oocyte quality and developmental competence. To discover any correlation of genes expression with the clinical parameters of patients, the efficacy of ovulation and the outcome of IVF or ICSI. To explore if the examnined genes could be molecular prognostic markers for embryo development to increase the chance of a successful pregnancy with assisted reproductive technologies by optimizing oocyte and embryo selection. **Design:** Prospective Clinical research study of patients undergoing IVF or ICSI. **Setting:** IVF Center, University Department of Obstetrics and Gynecology, “Alexandra” General Hospital, Athens and Research Laboratory, First Department of Internal Medicine, “Laiko” General Hospital, Athens, Greece. **Patient(s):** Women undergoing oocyte retrieval for IVF or ICSI after ovulation induction with gonadotropins gave written consent to participate in this study. Twenty nine women were examined for SURVIVIN gene expression and twenty one for OCT-4 and DAZL gene expression. The causes of infertility were male or tubal factor. **Intervention(s):** Controlled ovarian hyperstimulation, serum hormone level measurements, ultrasonographic scanning of ovarian follicles, oocyte retrieval after hCG administration and embryo transfer were performed. Cumulus–oocyte complexes were denuded separately and the

cumulus cells were analyzed for each patient separately. In all cases three embryos were transferred. **Material and Methods:** All of the patients were stimulated with standard GnRH analogue-recombinant FSH protocol. Total RNA was extracted from granulosa cells and was reverse transcribed into cDNA using specific designed primers for SURVIVIN, OCT-4 and DAZL. SURVIVIN mRNA, OCT-4 mRNA and DAZL mRNA in human granulosa cells were detected by RT-PCR using fluorescent probes. To determine the steady amount for SURVIVIN, OCT-4 and DAZL mRNA levels in granulosa cells, a quantitative competitive PCR (QC RT-PCR) was developed. The number of transcripts of studied target genes was normalized according to the number of transcripts of the internal standard genes ABL and G6PD. The respective quantitative ratio was determined by the density of each target to the internal standard: Survivin mRNA / ABL mRNA, OCT-4 mRNA / G6PD mRNA and DAZL mRNA / G6PD mRNA. **Main Outcome Measure(s):** The expression rates of SURVIVIN, OCT-4 and DAZL of granulosa cells surrounding the oocytes were determined in the studied patients. Many variables were analyzed: age, BMI, infertility causes, infertility duration, previous IVF/ICSI cycles, serum concentrations of FSH, LH, progesterone, AMH at the beginning of the menstrual cycle, serum PRL levels, as measured during one of the previous six months, serum 17 $\beta$ -estradiol levels on the 5th day of FSH treatment and on the day of hCG, duration of stimulation, total FSH dose used for ovarian stimulation, ovarian response, oocyte maturity, embryo quality (grade), good quality embryos score, fertilization and pregnancy rates. **Results:** ABL and SURVIVIN mRNA was detected in the granulosa cells in 93.1% (27/29). The median of SURVIVIN mRNA / ABL mRNA was 0.45 with intra-quarteral range from 0.22 to 2.94. The quantitative ratio of Survivin mRNA was significantly lower in normal women (male infertility factor) compared to women with tubal infertility factor ( $p=0.007$ , Wilcoxon rank-sum test). G6PD and OCT-4 mRNA was detected in the granulosa cells in 47.6% (10/21). The median of OCT-4 mRNA / G6PD mRNA was 1.75 with intra-quarteral range from 0.10 to 98.21. The OCT-4 mRNA expression was statistically significant correlated with the number of oocytes retrieved; when the OCT-4 mRNA expression was higher then more than six oocytes were retrieved ( $p=0.037$ , Wilcoxon rank-sum). No detection of DAZL mRNA was found in granulosa cells. The levels of expression of OCT-4 were not connected with the levels of expression of SURVIVIN (Spearman's  $\rho=0.429$ ,  $p=0.289$ ). There was no additional statistically significant correlation between the levels of SURVIVIN or OCT-4 expression and the estradiol levels or the dosage of FSH for ovulation induction or the number of dominant follicles aspirated or the clinical pregnancy rates respectively. There was no statistically significant correlation between the levels of SURVIVIN expression and the number of retrieved oocytes. No association was found between the presence or absence of OCT-4 mRNA expression in granulosa cells and the ovarian response to gonadotropin stimulation. Also, no influence on pregnancy was observed between presence and absence of OCT-4 mRNA expression in granulosa cells or accordingly to its expression levels. **Conclusions:** High levels of SURVIVIN mRNA expression in luteinized granulosa cells in cases with tubal infertility seems to be observed for possible protection from follicular apoptosis. A subpopulation of patients with low levels of SURVIVIN mRNA in granulosa cells might benefit with ICSI treatment to bypass possible natural barriers of the sperm-oocyte interactions. The expression of OCT-4 mRNA, which is a typical stem cell marker and the absence of expression of DAZL mRNA, which is a

typical germ cell marker, both increase the indications that a subpopulation of luteinized granulosa cells in healthy ovarian follicles (47.6%) consists of stem cells which are not originated from primordial germ cells. Increased number of oocytes retrieved seems to correlate to higher levels of OCT-4 mRNA expression. Oct-4 expression in luteinized granulosa cells seems not to be required for protection from apoptosis.

#### **D. Thesis for Master Degree of Science in “Minimally Invasive Surgery, Robotic Surgery and Telesurgery”**

**“Assessment of laparoscopic surgical skills acquired on laparoscopic virtual reality simulator compared to box trainer: an analysis of obstetrics-gynecology residents”**

**Michail Varras.**

**Body responsible:** National Kapodistrian University of Athens, Faculty of Health Sciences, Medical School.

**Background:** Laparoscopic surgery requires a very different set of psychomotor skills compared to open surgery, such as working in three-dimensional environment with two-dimensional view and four instead of six degrees of freedom, eye-hand coordination, depth perception and bimanual manipulation. Laparoscopic surgical training using laparoscopic box-trainers and laparoscopic virtual reality (VR) simulators overcomes these inherent differences and improves efficiency of learning and patient safety. The aim of this study was to compare the effectiveness of classic low-fidelity box-trainer and high-fidelity VR simulator and determine whether one has advantages over the other as training tool of inexperienced in laparoscopy residents in Obstetrics-Gynaecology for performing relatively simple laparoscopic procedures. **Materials and Methods:** This is a prospective, randomized, blinded, comparative trial that enrolled 20 residents in Obstetrics and Gynaecology with minimal laparoscopic experiences to participate in practical exercises with either LapVR simulator (group-A), or laparoscopic Box-Trainer (group-B). The candidates acted as their own control. Subjects within one group were not allowed to practice, on the opposing trainers. Initial teaching session was given to obtain all the participants familiarization on the VR simulator and they carried out laparoscopic salpingotomy and laparoscopic salpingectomy for ectopic pregnancy on the LapVR simulator (pretest). Performance was recorded by LapVR simulator for parameters such as total time taken, time of cautery used, total blood loss and economy of motion. The subjects were then randomized to either group-A or group-B for a series of laparoscopic exercises. The residents of group-A were practiced on LapVR simulator in laparoscopic peg transfer, clipping and cutting and certain parameters were assessed by LapVR simulator. The practical exercises on laparoscopic Trainer-Box were based in the tasks of laparoscopic “ovarian cystectomy” for ovarian cyst and laparoscopic “salpingotomy” for ectopic pregnancy and they were captured on DVD and scored for time and accuracy by a blinded expert investigator. After 2-day sessions lasting one and half hours each, all subjects were reassessed on the initial same procedures on LapVR simulator (post-test). Each subject completed a 5-point Likert-type questionnaire rating the training modalities about the face validity and their satisfaction at the end of the module. Improvements between the pre-test and post-test evaluations were compared between two groups using one way ANOVA

analysis and Whitney U test. **Results:** During training, subjects in group-A demonstrated statistically negative significance between the assessed parameters and the number of repetitions for the tasks of laparoscopic peg transfer, clipping and cutting. Also, the performances during these tasks in the last two attempts were significantly better than the first two, meaning that the practice on the LapVR simulator improves certain laparoscopic skills. In terms of the “laparoscopic ovarian cystectomy” on the laparoscopic Box-Trainer simulator the evaluation of the scores showed that there was a statistically significant correlation between the analysis parameters and number of repetitions concerning total time to complete the task, success within allowable time, total path length and minimal damage of the cystic wall. In terms of the “laparoscopic salpingotomy” for ectopic pregnancy on the laparoscopic Box-Trainer a statistically negative significance was noted between total time to complete the task or the total path length for both hands or the success within the maximum allowable time (< 10min) and the number of repetitions respectively. Success for a longitudinal incision correlated positively to the number of repetitions ( $p=0.031$ ). These findings indicate improved laparoscopic learning skills. Performance of the 2 groups was comparable before and after training for both laparoscopic procedures. The participants’ satisfaction according to the post-training questionnaire was high for the training modality as a whole and showed no differences between groups. **Conclusion:** The current study demonstrated high-levels of users’ satisfaction with the educational role of both LapVR and Box-Trainer simulators and neither LapVR simulator nor Box-Trainer showed any superiority over other for training laparoscopic skills to novice learners. We suggest that, laparoscopic training laboratories in laparoscopic training hospitals could include VR simulators as a reasonable alternative to Box-Trainer simulators for laparoscopic training of inexperienced residents in laparoscopy.

## E. SCIENTIFIC STUDIES

### (i) SCIENTIFIC PAPERS PUBLISHED AS COMPLETE PAPERS IN INTERNATIONAL JOURNALS

#### 1. *ras* gene mutations in human endometrial carcinoma.

**Varras MN**, Koffa M, Koumantakis E, Ergazaki M, Protopapa E., Michalas S., Spandidos D.A.

**Oncology (Basel) 1996, 53 (6):505-510.**

**IPP (Impact per Publication) (2015): 2.088**

#### **Abstract:**

The purpose of this study was to assess the extent of involvement of the *ras* oncogene activation by point mutations in endometrial carcinoma in the Greek population. The PCR technique was employed, followed by RFLP analysis to identify the point mutations in codon 12 of the K-*ras*, H-*ras* and N-*ras* genes. K-*ras* gene point mutations were detected in 8 of the 55 cases (15%) of primary endometrial carcinoma, H-*ras* in 4 (7.3%), while no mutations were found for the N-*ras* gene. No correlation was found between the presence of *ras* gene mutations and the clinicopathological parameters, or patient survival. The only association found was

between *H-ras* mutations and the FIGO stage of the tumor (Fisher's exact test,  $p = 0.011$ ). These results indicate a possible role of *ras* gene activation in a small subset of endometrial carcinomas.

**2. Glucorticoid and estrogen receptors have elevated activity in human endometrial and ovarian tumors as compared to the adjacent normal tissues and recognize sequence elements of the H-ras proto-oncogene.**

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Japanese Journal of Cancer Research 1996, 87:912-922, ISSN: 0910-5050**

**Continues as: Cancer Science (formerly Japanese Journal of Cancer Research), ISSN: 1347-9032, Online ISSN: 1349-7006**

**IPP (Impact per Publication) (2015): 3.547**

**Abstract:**

We examined the level of receptor binding in *H-ras* elements, using nuclear extracts derived from human endometrial and ovarian lesions and from adjacent normal tissue in gel retardation assays. We found increased binding of the glucocorticoid receptor (GR) to the *H-ras* GR element in more than 90% of endometrial tumors and in all ovarian tumors tested, as compared to the corresponding adjacent normal tissue. Additionally, we found elevated binding of the estrogen receptor (ER) in *H-ras* ER element in all pairs of ovarian tumor/normal tissue tested, whereas in ER-negative control breast tumor/normal tissue pairs, no differences in ER DNA-binding levels were observed. These results suggest that steroid hormone receptor binding could directly activate the *H-ras* oncogenic potency in human endometrial and ovarian lesions, providing additional evidence for the role of *H-ras* expression in hormonally responsive human cancers.

**3. The association of the H-ras oncogene and steroid hormone receptors in gynecological cancer.**

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Journal of Experimental Therapeutics and Oncology 1996, 1 (6):335-341.**

ISSN: 1533-869X (on line), ISSN: 1359-4117 (print).

**IPP (Impact per Publication) (2015): 1.349**

**Abstract:**

Expression of the *ras* family of cellular oncogenes is associated with tumorigenicity, invasiveness and metastatic potential in a variety of human carcinomas. Additionally, *H-ras* cooperates with glucocorticoids and with ovarian hormones in cell transformation and in the development of mammary carcinomas. Steroids are considered to be tumor promoters and their levels influence the cure rates and survival of the patients with gynecological lesions. It is proposed that they exert tumor promoting activity by transcriptional regulation of nuclear proto-oncogenes, such as *c-fos*, *c-jun*, and *c-myc*. The human *H-ras* gene contains within its first and fourth introns, sequences that are specifically recognized by glucocorticoid and estrogen receptors, respectively. Using gel retardation assays, the level of steroid receptor binding in *H-ras* elements has been compared, employing nuclear extracts from human endometrial and ovarian lesions and from the adjacent normal tissue.

Elevated binding of the glucocorticoid and estrogen receptors in the corresponding H-*ras* elements in almost all tissue pairs tested has been found. It is suggested that the H-*ras* proto-oncogene is hormonally regulated and directly implicated in human gynecological cancer through elevated, steroid-induced gene expression.

**4. Endometrial carcinoma in a breast cancer patient treated with tamoxifen: Activation of K-*ras* proto-oncogene.**

Varras M., Zachos G., Spandidos D.A.

[Oncology Reports 1997, 4:1045-1046.](#)

**IPP (Impact per Publication) (2015): 2.428**

**Abstract:**

The use of tamoxifen for breast cancer therapy is linked to an increased danger of developing endometrial neoplasias in postmenopausal patients receiving the drug. Understanding the molecular mechanisms of the tumorigenic activity of tamoxifen may be of great prognostic and therapeutic significance. Our study suggests that tamoxifen treatment and alterations of the K-*ras* proto-oncogene may occur as parallel events in carcinogenesis of the endometrium.

**5. Detection and clinical correlations of *ras* gene mutation in human ovarian tumors.**

Varras M.N., Sourvinos G., Diakomanolis E., Flouris G.A., Koumantakis E., Lekka-Katsouli I., Michalas S., Spandidos D.A.

[Oncology \(Basel\) 1999, 56 \(2\):89-96.](#)

**IPP (Impact per Publication) (2015): 2.088**

**Abstract:**

In epithelial ovarian neoplasms K-*ras* codon 12 gene mutations show a wide variation fluctuating between 4-39% in invasive carcinomas and 20-48% in borderline malignant tumors. In this study, we showed the pattern of point mutations in codon 12 of the K-*ras*, H-*ras* and N-*ras* genes, using polymerase chain reaction restriction fragment length polymorphism analysis in 74 tissue specimens of Greek patients with epithelial ovarian tumors. K-*ras* and H-*ras* gene mutations were detected in 11/48 (23%) and 3/48 (6%) cases with primary invasive ovarian carcinomas, respectively, while N-*ras* gene mutations were not found. No mutation of K-, H- and N-*ras* genes was detected in 23 ovarian cystadenomas. In 1 out of 3 borderline ovarian tumors (33%) we found an H-*ras* gene mutation. The prevalence of mutations in K-*ras* gene was 1/8 (13%) in mucinous, 7/29 (24%) in serous.

**6. *Ras* gene activation in malignant cells of human ovarian carcinoma peritoneal fluid.**

Dokianakis D.N., Varras M.N., Papaefthimiou M., Apostolopoulou J., Simiakaki H., Diakomanolis E., Spandidos D.A.

[Clinical & Experimental Metastasis 1999, 17 \(4\):293-297.](#)

**IPP (Impact per Publication) (2015): 2.851**

**Abstract:**

In this study, we showed, for the first time, the pattern of point mutations at codon 12 of the *K-ras*, *H-ras* and *N-ras* genes, using polymerase chain reaction and restriction fragment length polymorphism analysis in 47 malignant cytologic specimens of ovarian adenocarcinoma peritoneal fluids. Forty-seven % of the samples were found to carry a point mutation at codon 12 of *K-ras* gene. Also, 21 cystadenoma peritoneal fluids were used as control specimens for the detection of *ras* mutations. Fourteen % of these samples were found to carry a point mutation at codon 12 of the *K-ras* gene. The prevalence of *K-ras* gene mutations were statistically correlated with FIGO and surgical stage of the malignant specimens. Our data demonstrates that the *K-ras* gene mutations are mainly affected (47%) in the malignant cells of the peritoneal washings or ascites of women with ovarian adenocarcinomas and may have value for the early diagnosis and monitoring of these neoplasms.

### **7. Sclerosing stromal of the ovary: A case report and review of the literature.**

Stylianidou A., **Varras M.**, Akrivis Ch., Fylaktidou A., Stefanaki S., Antoniou N.

**European Journal of Gynaecological Oncology 2001, 22 (4):300-304.**

**IPP (Impact per Publication) (2015): 0.684**

#### **Abstract:**

Sclerosing stromal ovarian tumor is an extremely rare neoplasm occurring predominantly in the second and third decades of life. It presents most often with non-specific symptoms. We describe a new case occurring in a young woman presenting with infertility and irregular menses. Ultrasound examination showed a left heterogenous ovarian mass without focal calcifications. Histological features included a pseudolobular pattern with focal areas of sclerosis, prominent vascularity and a two-cell population of spindled and polygonal cells. Immunohistochemical analysis for actin, vimentin, laminin, vascular epidermal growth factor (VEGF), oestrogen and progesterone receptors using formalin-fixed and paraffin-embedded materials showed predominant positivity for a-smooth muscle actin and consistent positivity for laminin and vimentin. The epidermal VEGF demonstrated rich tumor vascularity. Oestrogen and progesterone receptors were not expressed suggesting hormonally independent development. Menstrual cycle disturbances, however, were corrected following extirpation of the tumor, indicating some endocrine involvement. In addition, the patient became pregnant ten months after the operation. The differential diagnosis is discussed.

### **8. Extramedullary hematopoiesis in the uterine isthmus: A case report and review of the literature.**

**Varras M.**, Stylianidou A., Akrivis Ch., Galanis P., Stefanaki S., Antoniou N.

**European Journal of Gynaecological Oncology 2002, 23 (3):227-230.**

**IPP (Impact per Publication) (2015): 0.684**

#### **Abstract:**

Extramedullary hematopoiesis (EH) is the ectopic production of myeloid, erythroid and megakaryocytic elements. In postfetal life it usually occurs in conditions with hyperactive, depleted or infiltrated marrow; it is extremely rare in the genital tract.

We report a case of EH in the uterine isthmus (UI) which was found incidentally in a 40-year-old patient who presented with a right ovarian cyst and a history of a right modified radical mastectomy for infiltrating invasive lobular carcinoma one year earlier. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Microscopic examination of UI revealed foci of hematopoiesis, consisting of white blood cell precursors confirmed by positive chloroacetate-esterase staining. Bone marrow biopsy showed diffuse infiltration secondary to breast cancer. Further work-up, including a bone scan, showed multiple metastases suggesting that the high degree of bone marrow infiltration by neoplastic cells had stimulated the EH. In conclusion, the unusual finding of EH in UI heralded widespread infiltration of bone marrow.

**9. Primary ruptured ovarian pregnancy in a spontaneous conception cycle: A case report and review of the literature.**

**Varras M.**, Polyzos D., Kalamara Ch., Antypa E., Tsikini A., Tsouroulas M., Antoniou S., Paissios P.

**Clinical and Experimental Obstetrics and Gynaecology 2002, 29 (2):143-147.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Ovarian pregnancy is an uncommon presentation of ectopic gestation, where the gestational sac is implanted within the ovary. Usually, it ends with rupture, which occurs before the end of the first trimester. Its presentation often is difficult to distinguish from that of tubal ectopic pregnancy and hemorrhagic ovarian cyst. We describe a case of primary ovarian pregnancy in a 31-year-old patient who presented to the emergency room with symptoms and signs of peritonism and positive urine hCG test. The gestation sac was demonstrated in the right ovary by transvaginal sonography. MSD (mean sac diameter) was 15 mm corresponding to the sixth gestational week. Free fluid was found in the Douglas pouch. Culdocentesis was positive for hemoperitoneum. Henceforth, emergency laparotomy and wedge resection of the ovary was performed. Aetiological, clinical and therapeutical aspects of this rare extrauterine pregnancy are described. Also, the problems of its differential diagnosis are discussed.

**10. Five-year survival of a patient with primary endometrial squamous cell carcinoma: A case report and review of the literature.**

**Varras M.**, Kioses E.

**European Journal of Gynaecological Oncology 2002, 23 (4):327-329.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Primary endometrial squamous cell carcinoma (PESCC) is an uncommon entity, with fewer than 100 cases reported in the English literature. Survival data for PESCC are not well reported and a precise five-year survival rate for PESCC has not been determined. This study focuses on the five-year survival of a 61-year-old patient with PESCC and adds information to an area which is not well documented. The patient

was treated by hysterectomy with bilateral salpingo-oophorectomy and assigned to FIGO stage Ib. No adjuvant therapy was given. During the 60-month follow-up period, the patient remained free of disease. This outcome suggests that in the early stage of PESCC, surgical treatment alone is adequate to arrest the disease.

**11. Endometriosis causing extensive intestinal obstruction simulating carcinoma of the sigmoid colon: A case report and review of the literature.**

**Varras M.**, Kostopanagiotou E., Katis K., Farantos Ch., Angelidou-Manika Z., Antoniou S.

**European Journal of Gynaecological Oncology 2002, 23 (4):353-357.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Endometriosis with intestinal serosal involvement is not uncommon in women of childbearing age, however, presentation as colon obstruction is rare. Lack of pathognomonic symptoms makes diagnosis difficult, the main problem being differential diagnosis with neoplasm, even intraoperatively. Reported here is a case of extensive bowel obstruction due to sigmoid colon endometriosis in a 43-year-old woman who presented with signs and symptoms of bowel obstruction. Barium enema showed sigmoid obstruction; subsequent exploratory laparotomy showed the sigmoid colon surrounded by fibrous tissue, leading to its angulation and extensive lumen obstruction. Left oophorectomy and radical resection of descending and sigmoid colon as for bowel carcinoma were successfully employed. Pathological examination revealed endometriosis in the bowel wall with preservation of the mucosa. Aetiology, clinical presentation, differential diagnosis and therapeutic options for intestinal obstruction due to endometriosis are discussed.

**12. Heterotopic pregnancy in a natural conception cycle presenting with tubal rupture: A care report and review of the literature.**

**Varras M.**, Akrivis Ch., Hadjopoulos G., Antoniou N.

**European Journal of Obstetrics Gynecology and Reproductive Biology 2003, Jan 10; 106 (1):79-82.**

**IPP (Impact per Publication) (2015): 1.776**

**Abstract:**

**BACKGROUND:** Heterotopic pregnancy is a potentially fatal condition, rarely occurring in natural conception cycles. **CASE:** We report such a case in a 28-year old para 0, gravida 1 woman with no known risk factors. The ectopic pregnancy was diagnosed after rupturing at 11 weeks, 4 weeks after diagnosis of the intrauterine pregnancy, and resected via laparotomy. A healthy baby was delivered without complications at 40 weeks gestation. **CONCLUSION:** Heterotopic pregnancy is possible with natural conception and the survival of the intrauterine fetus is feasible.

**13. Ultrasonographic and computed tomography manifestations of intussusception secondary to primary non-Hodgkin's lymphoma diagnosed in puerperium: Report of a case and review of the literature.**

Samara Ch., Tsikini A., Antoniou S., Polyzos D., **Varras M.**

**European Journal of Gynaecological Oncology 2002, 23 (6):569-572.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Non-Hodgkin's lymphoma is infrequently diagnosed during pregnancy and puerperium. A 21-year-old woman, para II, gravida II, on the seventh postpartum day arrived at the Emergency Gynaecologic Clinic complaining of colicky abdominal pain associated with bilious vomiting. A large tender mass of firm consistency was palpated in the midline towards the left hypochondrium. A CT scan of the upper abdomen showed thickened small bowel with halo, specifically at the junction of the jejunum with the ileum, resembling imaging of intussusception. Also, blocks of mesenteric and paraortic lymph nodes and multiple lymph nodes inducing enlargement of the anterior mediastinum were found. These findings rendered a picture of lymphoma in Stage at least III. Subsequent exploratory laparotomy confirmed our preoperative diagnosis. Histopathological examination of the lymph node biopsies established the diagnosis of a primary non-Hodgkin's lymphoma. Judging from the extent of the non-Hodgkin's lymphoma in our patient seven days after delivery the disease probably already existed during the last trimester of pregnancy. This study demonstrates a remarkable delay in diagnosis of non-Hodgkin's lymphoma in pregnancy. The diagnostic dilemmas of non-Hodgkin's lymphoma during pregnancy are emphasized and the literature is reviewed.

**14. Intraperitoneal haemorrhage secondary to perforation of uterine fibroid after cystic degeneration: Unusual CT findings resembling malignant pelvic tumor.**

**Varras M.,** Antoniou S., Samara Ch., Frakala S., Angelidou-Manika Z., Paissios P.

**European Journal of Gynaecological Oncology 2002, 23 (6):565-568.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Intraperitoneal haemorrhage is a rare complication of myomatous uterus. We present a case of a 37-year-old white nullipara who presented in the emergency room with acute, lower-abdominal pain which reportedly started after riding over a bump on a motorcycle. On examination, the abdomen was diffusely tender, with moderate spasm and rebound tenderness in both iliac fossae. Pregnancy test was negative. Computed tomography revealed a soft-tissue mass with cystic components and inhomogeneous appearance. Free fluid in the peritoneal cavity suggested ascites. The patient underwent an exploratory laparotomy. A ruptured, actively bleeding, subserosal, nonpedunculated, cystic degenerated uterine fibroid was found, as well as approximately two liters of free, bloodstained peritoneal fluid and clots. Subtotal hysterectomy without salpingo-oophorectomy was performed, followed by evacuation of the fluid and clots. The patient's postoperative course was uneventful. In conclusion, definitive, preoperative diagnosis of a perforated, haemorrhaging, uterine fibroid is difficult; exploratory laparotomy is both diagnostic and therapeutic in this rare, life-threatening condition.

**15. Primary small-cell carcinoma of the endometrium: Clinicopathological study of a case and review of the literature.**

**Varras M.**, Akrivis Ch., Demou A., Hadjopoulos G., Stefanaki S., Antoniou N.  
**European Journal of Gynaecological Oncology 2002, 23 (6):577-581.**  
**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

**BACKGROUND:** Small-cell carcinomas are almost always primary in the lungs and are highly malignant. These tumors may also occur in the female genital tract. However, primary small-cell carcinoma of the endometrium is extremely rare with very few cases reported in the English literature. This tumor may exhibit evidence of neuroendocrine differentiation and has a high propensity for systemic spread and poor prognosis. **CASE:** A 55-year-old postmenopausal woman with primary small-cell carcinoma of the endometrium, FIGO stage Ib, underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and sampling node biopsies of the parametrial spaces, followed by adjuvant combined chemotherapy. **CONCLUSION:** A case of small-cell carcinoma of the endometrium, is reported and its clinical, histological and immunohistochemical features are discussed.

**16. Effects of tamoxifen on the human female genital tract: Review of the literature.**

**Varras M.**, Polyzos D., Akrivis Ch.  
**European Journal of Gynaecological Oncology 2003, 30(2-3):117-121.**  
**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Tamoxifen is a non-steroidal triphenylethylene derivate, with clear antioestrogenic effects on the breast, that is orally administrated for the treatment of breast cancer and its prevention in a high-risk population. This article analyzes the effects of tamoxifen on the adult human female genital tract and considers its carcinogenicity in the gynaecological reproductive organs. It has been found that tamoxifen causes oestrogenic changes of the vaginal and cervical squammous epithelium and increases the incidence of cervical and endometrial polyps. The action of tamoxifen on the human endometrium in postmenopausal women is connected with simple oestrogenic effects including hyperplasia, while in others with endometrial cystic atrophy. In cases where tamoxifen induces endometrial polyps and hyperplasia, the extensive fibrosis accounts for difficulties in obtaining endometrial biopsy or resecting the polyps. In premenopausal patients tamoxifen disrupts the menstrual cycles and causes ovarian cysts, while in postmenopausal patients it induces ovarian cystic tumors and endometriomas. Also, postmenopausal patients treated with tamoxifen may develop endometriosis, adenomyosis and leiomyomata. In addition, randomized trials have shown a link between tamoxifen use in breast cancer patients and the development of endometrial carcinomas. Moreover, of note is the fact that the association of tamoxifen therapy with uterine mesenchymal neoplasms is higher than expected. In conclusion, the most worrying gynaecological side-effect of tamoxifen is the well-known increased risk of endometrial carcinomas. Women with breast cancer treated with tamoxifen should undergo annual gynaecological examination, but endometrial sampling should be obtained only in the event of endometrial bleeding.

**17. Ruptured tubo-ovarian abscess as complication of IVF treatment: Clinical, ultrasonographic and histopathologic findings.**

**M. Varras**, D. Polyzos, A. Tsikini, E. Antypa, D. Apessou, M. Tsouroulas

**Clinical and Experimental Obstetrics & Gynecology 2003, 30 (2-3): 164-168.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Tubeoovarian abscess is a rare complication of IVF treatment, which can be lethal on rupture. Hereby, we present a case of a ruptured tubo-ovarian abscess, following transvaginal ultrasound-guided oocyte retrieval for IVF and transcervical embryo transfer in a 38-year-old white female patient with five years of primary infertility who underwent aspiration of bilateral hydrosalpinges at the time of oocyte retrieval. This case suggests that the reactivation of latent pelvic infection due to a previous pelvic inflammatory disease (PID) was the possible route of infection after transvaginal ultrasound-directed follicle aspiration--transcervical embryo transfer. We conclude that physicians should consider the diagnosis of tubo-ovarian abscess in the differential diagnosis of abdominal pain, fever and leukocytosis after ovum retrieval and transcervical embryo transfer for IVF treatment. Preservation of the uterus and unaffected uterine adnexa should be attempted in such cases if future pregnancy is desired.

**18. Early ultrasonographic diagnosis of unruptured interstitial pregnancy: A case report and review of the literature.**

Ch. Akrivis, **M. Varras**, J. Kyparos, A. Demou, S. Stefanaki, N. Antoniou.

**Clinical and Experimental Obstetrics & Gynecology, 2003, 30 (1): 60-64.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Interstitial ectopic pregnancy occurs when the fertilized ovum implants in the interstitial portion of the fallopian tube, where it transverses the wall of the uterus from the cornua to the corner of the uterine cavity. Interstitial ectopic pregnancy is an infrequent type of ectopic pregnancy, occurring in 2% to 4% of all tubal pregnancies. It is a life-threatening condition because myometrium rupture tends to occur in the second trimester of pregnancy resulting in profuse bleeding. This paper concerns the ultrasonographic diagnosis of a 33-year-old, gravida 4, para 3 woman with unruptured interstitial pregnancy, diagnosed in the 7th week of pregnancy. Awareness and suspicion of such pregnancy are required for its early detection. A combination of the sensitive beta-hCG assays, a single serum progesterone measurement and transvaginal ultrasonography are the principle tools used to make the diagnosis. The diagnostic difficulties are also discussed.

**19. Primary postpartum haemorrhage due to a large submucosal nonpedunculated uterine leiomyoma: A case report and review of the literature.**

Ch. Akrivis, **M. Varras**, A. Bellou, E. Kitsiou, S. Stefanaki, N. Antoniou

**Abstract:**

The complications of leiomyomas during pregnancy are very rare and can be divided into those occurring during pregnancy, at delivery and in puerperium. We present an unusual complication of large submucosal nonpedunculated uterine leiomyoma in puerperium. The patient was a 32-year-old woman, gravida 2, para 1, who was admitted to our department from a private maternity clinic with a considerable drop in haemoglobin 23 hours after delivery of a healthy boy. The placenta had easily and spontaneously delivered. On admission to our department her haemoglobin was 6.3 g/dl. Pelvic examination disclosed the presence of fresh blood clots in the vaginal vault. A circular firm structure by 12 -cm, was noted within the external cervical os. This mass was immovable. Total abdominal hysterectomy without salpingo-oophorectomy was immediately performed and the patient's postoperative course was uneventful. In conclusion, in this patient the uterine leiomyoma obstructed the cervical os and prevented the passage of lochia resulting in haematometra, uterine atony and subsequent serious uterine haemorrhage. In such cases obstetricians and gynaecologists should proceed immediately with surgical intervention to avoid a life-threatening situation.

**20. Torsion of a non-gravid leiomyomatous uterus in a patient with myotonic dystrophy complaining for acute urinary retention: anaesthetic management for total abdominal hysterectomy.**

**M. Varras**, D. Polyzos, Ch. Alexopoulos, P. Pappa, Ch. Akrivis.

**Abstract:**

Torsion of a pregnant uterus is rare, but torsion of a non-pregnant uterus is extremely rare. Abdominal pain is the major symptom. Other symptoms include vaginal bleeding, urinary tract symptoms and gastro-intestinal manifestations. We present a case of a 37-year-old white nullipara who presented at the emergency room with acute urinary retention. Medical history revealed that the patient carried the disease of myotonic dystrophy, which was diagnosed two years before. Physical examination revealed a tender, distended bladder, which was easily catheterized, draining 900 ml of clear urine. The abdomen was soft with no muscle guarding or rebound tenderness. A palpable large dense mass occupying the cul-de-sac was found during bimanual examination. Abdominal ultrasound examination revealed a large intramural leiomyoma approximately 10-cm in diameter, in the posterior wall of the uterus, which repelled the bladder. In neurological examination the muscular tone and reflexes were reduced in the lower extremities. Myotonic phenomenon was not found. The patient was thought to suffer from myotonic dystrophy and therefore the possibilities for pulmonary and cardiac complications or malignant hyperthermia had to be kept in mind during the anaesthetic management. The

patient underwent an exploratory laparotomy and the uterus was found to have undergone a 60 degrees rotation along the corpus and the cervix uteri transition line. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. The intra- and postoperative course of the patient was uneventful. In conclusion, in this patient the uterine pathology (large leiomyoma) in combination with the disease of myotonic dystrophy seemed to be the predisposing factors for the torsion of the non-pregnant uterus. Also, the anaesthetic implications for total abdominal hysterectomy in myotonic dystrophy are discussed and the international literature is reviewed.

**21. Clinical considerations and sonographic findings of a large nonpedunculated primary cervical leiomyoma complicated by heavy vaginal haemorrhage: a case report and review of the literature.**

**M. Varras**, P. Hadjilira, D. Polyzos, A. Tsikini, Ch. Akrivis, M. Tsouroulas.

**Clinical and Experimental Obstetrics & Gynecology, 2003, 30 (2-3):144-146.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Leiomyomas of the uterine cervix are uncommon. Cervical leiomyomas in non-pregnant women rarely are of clinical significance and their complications include pressure effects on the bladder or urethra, degenerative phenomema and menorrhagia. We present a case of 46-year-old female, gravida 2, para 1 who was presented in the gynaecological emergency room with the chief complaint of profound vaginal bleeding over the previous three weeks with recent passage of clots. Pregnancy test was negative. She suffered from profound orthostatic hypotension and tachycardia. On examination, her abdomen was soft, non-tender, and without rebound, guarding or palpable masses. Bimanual examination was notable for the presence of a large firm mass fixed to the uterine cervix. The cervix was 8 cm dilated and the body of the uterus was felt separate from the mass. The sonographic findings were consistent with a large cervical leiomyoma. Subtotal hysterectomy with salpingo-oophorectomy was performed and the patient's postoperative course was uneventful. In conclusion, in the present case the cause of the heavy vaginal bleeding was a primary cervical fibroid as the uterus attempted to abort it.

**22. Tubo-ovarian abscesses: spectrum of sonographic findings with surgical and pathological correlations.**

**Varras M.**, Polyzos D., Perouli E., Noti P., Pantazis I., Akrivis Ch.

**Clinical and Experimental Obstetrics and Gynecology, 2003, 30(2-3):117-121.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**OBJECTIVE:** Pelvic inflammatory disease (PID) is a serious condition that can lead to abscess formation. The purpose of this study was to identify the different sonographic markers on gray scale and color Doppler sonography in tubo-ovarian

abscesses. **MATERIAL AND METHODS:** The study group consisted of 25 women in whom the presence of tubo-ovarian abscess was confirmed by surgery and histopathology and their ultrasound records were analyzed retrospectively. **RESULTS:** Presence of a mass was found in all cases. The maximum diameter of the mass was 5-cm in two cases and between 5-cm and 10-cm in 23 cases. The mass was demonstrated at the anatomic position of the ovary in 21 cases (84%) and at the cul-de-sac in four cases (16%). The mass was a simple cyst in two cases (8%), in four cases it was cystic with diaphragms (16%), in four cases it was a thickened tube-shaped structure with multiple internal echoes (16%) and in 15 cases it was a mixture of cystic and solid elements (60%). Pyosalpinges with fluid-fluid levels were found in two cases. Fluid in the cul-de-sac was observed at a rate of 48%. Color Doppler sonography demonstrated abundant blood flow in the borders and the septa of the tuboovarian abscesses in 90% of the studied cases. **CONCLUSION:** The ultrasonographic findings of tubo-ovarian abscesses are not specific. The presence of a mass at the anatomic position of the ovary or at the cul-de-sac in combination with an increased number of white blood cells, elevated erythrocyte sedimentation rate and clinical findings are helpful for a correct diagnosis. Also, the color Doppler flow can further characterize the nature of the pelvic mass by detecting a significant rich blood flow in most cases of tuboovarian abscesses.

### **23. Prenatal diagnosis of congenital cystic adenomatoid lung malformation: a case report and review of the literature.**

Ch. Akrivis, **M. Varras**, A. Demou, A. Bellou, S. Stefanaki, N. Antoniou

[Clinical and Experimental Obstetrics and Gynaecology, 2003 30\(4\):259-262.](#)

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

#### **Abstract:**

Congenital cystic adenomatoid malformation of the fetal lung is an extremely rare developmental abnormality characterized by excessive overgrowth of the terminal respiratory bronchioles at the expense of the saccular spaces. We present a case of a 33-year-old, gravida 2, para 1, woman with congenital cystic adenomatoid lung malformation-type II diagnosed by ultrasound at the 20th week of gestation. On the right side of the chest an area with a maximum diameter of 18.5 mm and with small cystic lesions was recognized. The maximum diameter of the cysts was 0.5 cm. There were no other fetal abnormalities. The pregnancy was terminated and the postmortem examination confirmed the ultrasonographic findings. The cysts had the appearance of bronchiolus-like structures and were lined with cuboidal and columnar epithelium. Distended alveoli were present, while the airways were normal in structure. No other congenital anomalies were found. In conclusion, in this study we describe the ultrasonographic and pathologic findings of an unusual case of congenital cystic adenomatoid malformation of the fetal lung.

### **24. Mucinous cystadenoma of the ovary with functioning stroma and virilization in pregnancy: a case report and review of the literature**

N. Antoniou, **M. Varras**, Ch. Akrivis, A. Demou, A. Bellou, S. Stefanaki

[Clinical and Experimental Obstetrics and Gynaecology, 2003 30\(4\):248-252.](#)

**Abstract:**

Virilization caused by ovarian tumors with functioning stroma during pregnancy is extremely rare and has been reported in many ovarian tumors. In mucinous cystadenomas with maternal virilization during pregnancy the stromal cells responsible for the hormone secretion resemble lutein or Leydig cells and have been referred to as luteinized stromal cells. We present a case of a 30-year-old, gravida 2, para 1, woman who presented at approximately the 38th week of pregnancy with features of virilization. At the same time, a cesarean section was performed because of fetal distress and a male weighing 3,030-g without any gross abnormalities was delivered. A large tumor of the right ovary was detected and a right salpingo-oophorectomy was performed. Histopathologically, the tumor proved to be a benign mucinous cystadenoma. Masses typically resembling lutein stromal cells or Leydig cells of the testes or ovarian hilus were found in the wall of the cyst below the mucinous epithelium. No crystalloids of Reinke were identified. The stromal component of the tumor was characterized as functioning stroma with luteinized stromal cells. The glandular mucinous epithelium showed focal positivity for human chorionic gonadotrophin. The cytoplasm of the luteinized stromal cells reacted strongly and diffusely with antiserum for vimentin. Also, the cytoplasm of the luteinized stromal cells showed focal intense positivity for synaptophysin, and focal mild positivity for human chorionic gonadotrophin. Staining results for oestrogen and progesterone receptors were negative. In conclusion, we present an unusual case of clinical virilization during pregnancy associated with an ovarian mucinous cystadenoma with functioning stroma. The virilizing manifestations disappeared after removal of the ovarian neoplasm, supporting the perception that the functioning ovarian stroma was responsible for the androgen production.

**25. Action of 25µg 17beta-oestradiol vaginal tablets in the treatment of vaginal atrophy in Greek postmenopausal women.**

Ch. Akrivis, **M. Varras**, A. Thodos, G. Hadjopoulos, A. Bellou, N. Antoniou

**Clinical and Experimental Obstetrics and Gynaecology, 2003 30(4):229-234.**

**Abstract:**

**PURPOSE:** To evaluate the clinical efficacy and safety of intravaginal application of 25 microg micronized oestradiol in postmenopausal women from the Greek population suffering from symptoms related to vaginal atrophy. **MATERIALS AND METHODS:** 91 women suffering from vaginal dryness, vaginal itching and dyspareunia were treated with 25 microg 17beta-oestradiol vaginal tablets. The duration of treatment was 12 weeks. During the first two weeks the women inserted one vaginal tablet intravaginally once daily. Thereafter, the women inserted one tablet twice per week with at least a 3-day interval between treatments to maintain therapeutic response for ten weeks. Efficacy was evaluated by the relief of vaginal symptoms and safety by the concentrations of serum oestradiol (E2) and follicular-

stimulating hormone (FSH). Pretreatment and post-treatment findings were compared and each patient served as her own control. **RESULTS:** The rates of symptoms of vaginal dryness, vaginal itching and dyspareunia showed statistically significant differences over the course of the trial (Cochran Q test,  $p < 0.001$ ). No one complained of vaginal dryness and vaginal itching after four and six weeks of treatment respectively, while in one patient the sensation of dyspareunia remained constant after the fourth week of treatment. Despite the statistically significant increase in blood oestradiol levels in relation to baseline values (ANOVA model of repeated measures,  $p < 0.001$ ), these levels were within the normal range for postmenopausal women. Also, serum FSH levels were statistically significantly reduced from 47.4 mIU/ml at entry into the study to 45.5 mIU/ml after two weeks of treatment (dependent samples t-test,  $p < 0.003$ ), but were clearly within the postmenopausal range. **CONCLUSIONS:** The twice-weekly local single treatment with vaginal tablets containing 25 microg of 17beta-oestradiol was effective and safe for the relief of symptoms related to atrophic vaginitis in postmenopausal women from the Greek population.

**26. Large endometrial polyp with sarcomatous stromal components following long-term tamoxifen treatment for breast cancer: a case report and review of the literature.**

**M. Varras**, Ch. Akrivis

[European Journal of Gynaecological Oncology 2003;24\(6\):565-8.](#)

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Tamoxifen is commonly used in the management of patients with breast cancer because of its anti-oestrogenic effects to the breasts. However, tamoxifen acts as an oestrogen agonist on the endometrium increasing the incidence of endometrial polyps, hyperplasia and cancer. In addition, it may be possible that tamoxifen increases the occurrence of uterine body tumours. We describe a rare case of a large endometrial polyp with sarcomatous stromal components in a 73-year-old breast cancer patient treated daily with 20 mg of tamoxifen for four years. The glands of the polyp were lined by benign appearing epithelium. The polyp was twisted and protruded from a dilated cervix at the entrance of the vagina. The patient was treated by removal of the polyp and dilatation and curretage. A postoperative computed tomography scan showed many focal hypodense lesions in the hepatic lobes with a well-defined profile suggestive of metastatic disease and the patient was referred for combined chemotherapy. In conclusion, a case of a mesenchymal malignant neoplasm arising in the uterus of a breast cancer patient treated with tamoxifen is reported and its clinical, histological and immunohistochemical features are discussed. Also, the international literature is reviewed.

**27. A voluminous twisted paraovarian cyst in a 74-year-old patient: case report and review of the literature.**

**M. Varras**, Ch. Akrivis, D. Polyzos, S. Frakala, Ch. Samara

[Clinical and Experimental Obstetrics and Gynaecology 2003 30\(4\):253-256.](#)

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Although paraovarian cysts rarely cause symptoms, they may be complicated due to massive size, torsion or internal haemorrhage from rupture. Moreover, benign or malignant neoplasms may occasionally develop in paraovarian cysts. The risks from voluminous ovarian or paraovarian cysts are due to severe cardiovascular, pulmonary, and circulatory problems including surgical and postoperative complications. We present a case of a 74-year-old patient who suffered from a twisted voluminous right paraovarian cyst. Her preoperative respiratory function required attention. The patient was treated surgically with good results and she showed notable improvement of her respiratory function, postoperatively. The maximum diameter of the mass was 26 cm and its total weight was 5,100 g. In addition, a simple cyst was found in the left ovary with a maximum diameter of 9.5 cm and total weight of 300 g. In conclusion, paraovarian cysts, even in elderly patients, can reach large sizes requiring awareness of the problems that these large masses may cause.

**28. Internal haemorrhage caused by a twisted malignant ovarian dysgerminoma: Ultrasonographic findings of a rare case and review of the literature.**

**M. Varras**, A. Tsikini, D. Polyzos, Ch. Samara, Ch. Akrivis

**Clinical and Experimental Obstetrics and Gynaecology 2004;31(1):73-8.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**PURPOSE:** Ovarian cancer presents as an acute abdomen very rarely. The purpose of the study is the description of a right ovarian malignant dysgerminoma presenting as an abdominal emergency. **CASE:** A 16-year-old white female presented with acute abdominal pain in the right iliac fossa. On physical examination the abdomen was acute and a mass in the right lower abdomen was palpated. The patient was sexually active and bimanual gynecological examination revealed the presence of a large lobulated solid tumor in the position of the right adnexa. Ultrasound examination showed the presence of a large, multilobulated, heterogeneous, predominantly solid pelvic mass. Color flow imaging showed intratumoral flow signals. The uterus and the left ovary had normal size and echo-texture. Fluid was found in the cul-de-sac and in Morisson's space. An immediate exploratory laparotomy exposed the presence of a twisted right ovarian mass and intraperitoneal hemorrhage. A superficial tumoral vessel actively bleeding was seen. Peritoneal fluid was obtained for cytology. The intra-abdominal hemorrhage ceased when the ovarian pedicle was clamped. The patient underwent right salpingo-oophorectomy and biopsy of the omentum. Pathologic analysis revealed a malignant dysgerminoma of the right ovary, expanding to the mesosalpinx. Cytology was positive for malignancy. Postoperative CT scan of the upper and lower abdomen was negative. The patient was assigned to FIGO Stage IIC and referred for platinum-based chemotherapy. **CONCLUSION:** Ovarian malignant dysgerminoma may present as an acute abdomen because of torsion, passive blood congestion, rupture of superficial tumoral vessels

and subsequent intra-abdominal hemorrhage. Ovarian dysgerminoma should be part of the differential diagnosis in a young woman with acute surgical abdomen and a solid heterogeneous pelvic mass detected by ultrasonographic scan.

**29. Uterine adnexal torsion: pathological and gray-scale ultrasonographic findings.**

**M. Varras**, A. Tsikini, D. Polyzos, Ch. Samara, G. Hadjopoulos, Ch. Akrivis

**Clinical and Experimental Obstetrics and Gynaecology 2004;31(1):34-8.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**INTRODUCTION:** Uterine adnexal torsion is a rare and potentially lethal condition that may arise most unexpectedly in women of any age. It may be partial or complete, the later often resulting in necrosis, gangrene and peritonitis if untreated. The purpose of the study was to determine the spectrum of the histologic and gray-scale sonographic pictures in a series of surgically proven cases of uterine adnexal torsion. **METHODS:** The study population for the pathologic analysis of twisted uterine adnexa included 92 patients with surgical confirmation of torsion of the uterine adnexa; all the patients were treated radically. All the pathology records were reviewed retrospectively over a 10-year period (from 1992 to 2002) by the coding of ovarian, fallopian tube or adnexal torsion. The gray-scale sonographic findings were analysed in 20 patients who underwent sonographic examination before surgery and adnexal torsion was confirmed at surgery. **RESULTS:** Neoplasms constituted 46% (42/92) and cysts formed 48% (44/92) of all the twisted uterine adnexa. Normal-sized twisted adnexa were found in five patients (5%) while in one patient simultaneous torsion of both normal fallopian tubes was found (1%). The prevalence of the twisted neoplasms was 16 mature teratomas, nine serous cystadenomas, five mucinous cystadenomas, three serous borderline carcinomas, two fibroma/thecomas, two mucinous borderline carcinomas, two malignant granulosa-stromal cell tumours, one malignant dysgerminoma, one immature teratoma and one clear cell adenocarcinoma. The twisted cysts were 18 serous cysts, 11 paraovarian cysts, nine corpus luteum cysts, three hydrosalpinges, one mucinous cyst and one endometrioma. In one case the torsion of the right ovary was due to hyperstimulation of the ovaries with gonadotropin therapy for IVF treatment. Gray-scale sonographic examination demonstrated cystic lesions in 80% (16/20), solid masses in 5% (1/20) and normal adnexa in 15%; cul-de-sac fluid was present in 55% (11/20). Laparotomy revealed reactive cul-de-sac fluid in ten of these cases (50%) and haemoperitoneum in one (5%). **CONCLUSION:** Adnexal torsion is most commonly associated with benign processes (89%) and usually occurs in patients under 50 years old (80%). The spectrum of sonographic findings varies due to the adnexal pathology, the degree and the duration of adnexal torsion.

**30. Benefits and limitations for ultrasonographic evaluation of uterine adnexal lesions in early detection of ovarian cancer.**

**M. Varras**

**Clinical and Experimental Obstetrics and Gynaecology 2004, 31, 85-98.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Ovarian cancer is the most frequent cause of death from gynaecological malignancies in the Western world. Most cases of epithelial ovarian cancer are detected at late stages and the resultant overall five-year survival is poor. However, when epithelial ovarian cancer is detected with the disease confined to the ovary the prognosis is favorable. Transvaginal gray-scale ultrasonography and colour Doppler assessment of blood flow have been evaluated as methods to predict risk of malignancy in ovarian tumours. In order to reduce the number of unnecessary surgical procedures for uterine adnexal tumours, ultrasonomorphologic scoring systems have been developed, assigning numerical ultrasonographic parameters of the tumours. However, the positive predictive value of these scoring systems is low and this is due to the fact that the appearance of many benign ovarian lesions overlaps with that of malignant disease. In addition, some ovarian malignancies are ultrasonographically detected as simple cysts without exhibiting a complex morphology. Moreover, the cut-off size of uterine adnexal tumours for surgical intervention in the early detection of cancer is not yet well determined. The application of colour blood-flow imaging is very helpful in the detection of uterine adnexal malignancy because of the presence of neovascularization in malignant tumours. When gray-scale ultrasonography detects the presence of septum or papillary projections or solid components in uterine adnexal lesions and Doppler flow is present within these lesions malignancy is likely. However, the detection of vascularity within the papillary projection of a malignant tumour may not be detected when it is very small. When colour-flow imaging is used in premenopausal patients attention is needed to avoid confusion of luteal flow with flow of cystic lesions. Initial reports using pulsed Doppler ultrasonography showed high sensitivity and specificity in the detection of ovarian cancer when levels of the resistive index (RI) less than 0.4 and levels of the pulsatility index (PI) less than 1 were used. Subsequent studies have shown considerable overlap of RI and PI rates between benign and malignant uterine adnexal masses, suggesting that pulsed Doppler ultrasonography is not an independent indicator for malignancy. Serum CA-125 levels have been used in conjunction with ultrasonography to identify as many of the false-positive results in order to avoid unnecessary surgery. In postmenopausal women with a uterine adnexal mass the combination of physical examination with serum CA-125 levels and pelvic ultrasound scan seems to improve the sensitivity and specificity of predicting adnexal malignancies. In contrast, in premenopausal women the consideration of CA-125 levels with Doppler ultrasonographic findings might confuse the differential diagnosis of ovarian masses. In conclusion, accurate selection of patients with uterine adnexal tumours for surgical intervention is not provided by pelvic ultrasonography. Pelvic ultrasonography as a screening method for the early detection of ovarian cancer should be probably limited to those women who are at increased risk for development of ovarian cancer and not in the general population.

**31. Intraperitoneal bupivacaine for the reduction of postoperative pain following operative laparoscopy: a pilot study and review of the literature.**

Buck L, **Varras MN**, Miskry T, Ruston J, Magos A.  
**Journal of Obstetrics and Gynaecology 2004, 24(4):448-451.**  
(ISSN: 01443615, 13646893)  
**IPP (Impact per Publication) (2015): 0.705**

**Abstract:**

This pilot case-control study was carried out to determine the value of intraperitoneal irrigation with a long-acting local anaesthetic agent in reducing postoperative analgesic requirements following gynaecological operative laparoscopy. Twenty women undergoing gynaecological laparoscopic surgery were recruited to receive dilute bupivacaine instilled into the peritoneal cavity at the completion of surgery. Analgesic requirements were assessed during the first 10 hours, and pain scores at 4 and 24 hours. Analgesic requirements were then compared with historical controls. Our results revealed that the total parenteral opioid requirement after bupivacaine was significantly less than in the control group (0.50 mg vs. 7.17 mg, P=0.006). Oral analgesic requirements were not significantly different between the two groups. Pain scores in the bupivacaine group showed no difference at 4 and 24 hours postoperatively. Intraperitoneal irrigation with dilute bupivacaine at the end of gynaecological laparoscopic surgery appears to reduce early postoperative analgesic requirements in this pilot study.

**32. Primary fallopian tube adenocarcinoma: Preoperative diagnosis, treatment and follow-up.**

**M. Varras**, Ch. Akrivis, A. Bellou, V.D. Malamou-Mitsi, N. Antoniou, C. Tolis, E. Salamalekis  
**European Journal of Gynaecological Oncology 2004, 25 (5):640-646.**  
**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Preoperative diagnosis of fallopian tube carcinoma is difficult due to the rarity and silent course of this neoplasm. We present herein the case of a 58-year-old woman with primary fallopian tube carcinoma that was diagnosed preoperatively on the basis of a positive for adenocarcinoma Papanicolaou vaginal smear, repeated episodes of vaginal bleeding, negative endocervical and endometrial curettage, characteristic features on ultrasonography and elevated CA-125 levels. The patient was treated by total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy. Pathologic confirmation of primary serous papillary adenocarcinoma of the left fallopian tube was made. Peritoneal washings were positive for malignancy. FIGO stage was considered as IIIb and the patient received six courses of combined carboplatin-taxol chemotherapy. At two years from onset of therapy the patient underwent a modified radical mastectomy and lymphadenectomy because of primary carcinoma of the right breast. The patient was started on tamoxifen therapy, which she is still taking. At 60 months after initial surgery, the patient is alive and well. In conclusion, our study suggests an association between fallopian tube carcinoma and breast cancer and a good response of the patient to platinum-based chemotherapy.

**33. Primary ovarian carcinosarcoma: a case report and review of the literature.**

**M. Varras**, Ch. Akrivis, N. Antoniou, Tolis C. , S. Stefanaki, E. Salamalekis  
**European Journal of Gynaecological Oncology 2004, 25 (5):653-656.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Primary ovarian carcinosarcoma is characterized by an admixture of malignant epithelial and stromal elements. This neoplasm is extremely rare with fewer than 400 cases reported in the English literature. Its histogenesis, clinical features and optimal treatment remain unclear because of the rarity of primary ovarian carcinosarcoma. This study focuses on the clinical, pathological, immunohistochemical features and survival of a 73-year-old patient with primary ovarian carcinosarcoma. The patient was treated with surgery followed by combined chemotherapy with carboplatin and taxol and assigned to FIGO Stage IIIc. She died from the disease 17 months after surgery. In conclusion, ovarian carcinosarcoma is a very aggressive tumor, especially when it is diagnosed at advanced stage.

**34. Isolated torsion of the fallopian tube: a case report and review of the literature.**

N. Antoniou, **M. Varras**, Ch. Akrivis, E. Kitsiou, S. Stefanaki, E. Salamalekis  
**Clinical and Experimental Obstetrics and Gynaecology 2004;31(3):235-8.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**INTRODUCTION:** Isolated torsion of the fallopian tube is a very rare condition. It occurs without ipsilateral ovarian involvement associated with pregnancy, haemosalpinx, hydrosalpinx, ovarian or paraovarian cysts and other adnexal alterations or even with an otherwise normal fallopian tube. We document a case of isolated torsion of the right fallopian tube associated with hydrosalpinx. **CASE:** The patient was a 39-year-old female, para 2, gravida 4, who was presented with acute pelvic pain, nausea and vomiting. Her medical history included an appendectomy and right hydrosalpinx diagnosed five months before admission by hysterosalpingography because of investigation for secondary infertility. The urinary pregnancy test was negative. Pelvic ultrasonography showed a dilated folded right tubular structure measuring 7.8 x 2.7 cm with thickened echogenic walls and mucosal folds protruding into the lumen; the ovaries and uterus were unremarkable. No free fluid in the cul-de-sac was noted. Preoperatively, a diagnosis of twisted right fallopian tube was suspected and an exploratory laparotomy confirmed the diagnosis of isolated torsion of the oviduct. The ipsilateral ovary appeared normal, but the fallopian tube was gangrenous and right salpingectomy was performed. The patient became pregnant three months after surgery. **CONCLUSION:** Isolated torsion of the fallopian tube should be considered in the differential diagnosis of patients with acute abdomen and previous medical history of hydrosalpinx.

**35. The problems with different management options of women with minor squamous intraepithelial lesions in Pap tests.**

**M. Varras - EDITORIAL**

**Clinical and Experimental Obstetrics and Gynaecology 2004, 31 (4):249-250.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

The optimum management of women with minor squamous intraepithelial lesions in Pap tests is controversial. With cytological surveillance after one Pap test showing atypical cells of undetermined significance (ASCUS), a significant proportion of women will have undiagnosed squamous intraepithelial lesions. On the other hand, using immediate colposcopy for ASCUS almost half of the women would not have needed the procedure. This number for referral for colposcopy can be reduced to only those women who test positive for high-risk HPV-DNA, however some women will have undiagnosed squamous intraepithelial lesions. In addition, when surveillance with repeat Pap tests is used for the management of low-grade cervical squamous intraepithelial lesions (LSIL) a significant number of high-grade cervical intraepithelial lesions can be missed. In this article all the problems of each management policy in women with minor squamous intraepithelial lesions in Pap tests are addressed.

**36. Multiple dermoid cysts within the same ovary: our experience of a rare case with review of the literature.**

N. Bournas, **M. Varras**, D. Kassanos, Ch. Chrelas, O. Tzaida, E. Salamalekis

**Clinical and Experimental Obstetrics and Gynaecology 2004, 31 (4): 305-308.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**OBJECTIVE:** Ovarian dermoid cysts are relatively frequent ovarian lesions that can be easily diagnosed by transvaginal ultrasonography. However, the recognition of multiple dermoid cysts, separated by normal ovarian tissue, within a single ovary is rare. **CASE:** We present a case with bilateral dermoid cysts, four dermoid cysts within the right ovary and one in the contralateral ovary. Transvaginal ultrasonography showed hyperechogenic areas in the right ovary with a hypoechogenic area in front of them; the hyperechogenic areas were separated by areas with the echogenicity of normal ovarian tissue and indentation, suggesting the presence of multiple dermoid cysts within the same ovary. **CONCLUSION:** Preoperative ultrasonographic suspicion of multiple dermoid cysts within the same ovary might contribute to a better decision about the surgical approach.

**37. Asynchronous bilateral uterine adnexal torsion in a 13-year-old adolescent: our experience of a rare case with review of the literature.**

**M. Varras**, Ch. Akrivis, A. Demou, N. Antoniou

**Journal of Adolescent Health 2005 Sep; 37(3):244-7.**

**IPP (Impact per Publication) (2015): 3.410**

**Abstract:**

Adnexal torsion is a serious condition and delay in surgical intervention may result in loss of the tube and/or ovary. Children and adolescents who have suffered from uterine adnexal torsion may be at risk for asynchronous torsion of the contralateral uterine adnexa. We report the case of sequential bilateral torsion of uterine adnexa in a 13-year-old girl, resulting in right and subsequently left salpingo-oophorectomy because of gross evidence of total necrosis in both uterine adnexa. After the castration the patient was started on hormone replacement therapy. Families of children who suffered from ovarian torsion and unilateral ovarian loss should be educated about the risk of the contralateral ovary for future torsion and should be encouraged to seek immediate medical help with the recurrence of abdominal pain.

**38. Ultrasonographic evaluation of a uterine malignant melanoma presenting as large pelvic mass.**

**M. Varras**, D. Kassanos, O. Tzaida, N. Bournas, N. Panagiotopoulos, Ch. Chrelas, E. Salamalekis

**Journal of Clinical Ultrasound 2005 Oct; 33(8):424-6.**

**IPP (Impact per Publication) (2015): 0.784**

**Abstract:**

The uterus is an extremely rare location for a primary or metastatic melanoma. We describe the ultrasonographic appearance of a malignant melanoma of the uterus presenting clinically as a large mass in a 78-year-old woman. Transabdominal sonography revealed a solid uterine mass measuring 13 x 11.5 x 8.5 cm with inhomogeneous echotexture and bright internal echoes. The tumor showed a diffuse spread inside the uterine corpus, and the endometrium was not demonstrated ultrasonographically.

**39. Angiomyofibrosarcoma of the vagina in a postmenopausal breast cancer patient treated with tamoxifen: clinicopathological analysis of a case and review of the literature.**

**M. Varras**, Ch. Akrivis, A. Demou, E. Kitsiou, N. Antoniou.

**International Journal of Gynecological Cancer 2006 Mar-Apr; 16(2):581-5.**

**IPP (Impact per Publication) (2015): 2.091**

**Abstract:**

Angiomyofibrosarcoma is a rare mesenchymal tumor. This study presents the clinical, histologic, and immunohistochemical features of an angiomyofibrosarcoma of the vagina occurring in an 80-year-old breast cancer patient under prolonged treatment with tamoxifen. Histologically, the tumor was characterized by alternating hypercellular and hypocellular edematous zones and small- to medium-sized blood vessels, which were characteristically thin walled. The tumor cells were spindle shaped (mainly) or round shaped (occasionally) arranged in cords and nests. The stroma was edematous and contained inflammatory cells, especially lymphocytes and mast cells. Immunohistochemistry of the tumor cells revealed diffuse and intense immunoreactivity for vimentin and desmin. The staining for estrogen receptors and progesterone receptors was positive, with a percentage of 70% and 40%, respectively. In conclusion, the tumor was diagnosed as an

angiomyofibroblastoma based on its typical histologic and immunohistochemical features. The expression of estrogen and progesterone receptors suggests that it might arise as a neoplastic proliferation of hormonally responsible mesenchymal cells. Tamoxifen may exert stimuli effects upon mesenchymal cells.

**40. Aggressive angiomyxoma of the vulva: a case report with review of the literature.**

**M. Varras**, Ch. Akrivis, P. Lekkou, E. Kitsiou, A. Demou, N. Antoniou.

**European Journal of Gynaecological Oncology 2006; 27(2):188-92.**

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

Aggressive angiomyxoma is a rare, benign but locally aggressive mesenchymal neoplasm, which occurs almost exclusively during the reproductive years of women. A 28-year-old woman developed an aggressive angiomyxoma within the left labium minus of the vulva. The tumor was excised, but the lesion was expanded to the surgical margins. Microscopically, sections showed many walled vessels of various sizes, a loose myxoid and collagenous stroma and stellate and spindle-shaped neoplastic cells. Immunohistochemically, the neoplastic cells showed strong positivity for vimentin and desmin and moderate positivity for CD34 and estrogen receptors. In conclusion, aggressive angiomyxoma of the vulva should be distinguished from the benign and malignant myxoid tumors or tumor-like conditions of vulva. The pathologic and immunohistochemic characteristics, the difficulties in determining the surgical margins and the treatment of this tumor are discussed. Also, the international literature is reviewed.

**41. Double vagina and cervix communicating bilaterally with a single uterine cavity: report of an unusual congenital uterine malformation and review of the literature.**

**M. Varras**, Ch. Akrivis, A. Demou, E. Kitsiou, N. Antoniou

**Journal of Reproductive Medicine 2007 Mar;52(3):238-40.**

**IPP (Impact per Publication) (2015): 0.784**

**Abstract:**

**BACKGROUND:** The existence of a longitudinal vaginal septum with double cervix communicating bilaterally with a nonseptate uterine body and normal adnexa is an unusual mullerian anomaly. **CASE:** A 43-year-old woman presented with menorrhagia and duplication of the cervix and vagina. A fibromatous uterus was suggested by clinical examination and confirmed by ultrasonography. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. The surgical specimen revealed a fibromatous uterus with double cervix communicating bilaterally with a nonseptate uterine body; both adnexa were normal. **CONCLUSION:** This rare mullerian anomaly is inconsistent with the classical embryologic theory of caudal to cranial mullerian development but supports the alternative embryologic hypothesis suggested by Muller et al, according to which fusion and absorption begin at the isthmus and proceed simultaneously in both the cranial and caudal directions.

**42. Tubal ectopic pregnancy associated with an extraskeletal chondroma of the fallopian tube: A case report.**

**M. Varras**, Ch. Akrivis, G. Tsoukalos, Ch. Plis, St. Karadaglis, I. Ladopoulos

[Clinical and Experimental Obstetrics and Gynaecology 2008, 35 \(1\): 83-85.](#)

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Extraskeletal chondroma is a relatively uncommon benign soft tissue tumor, which usually occurs in hands and feet. The tumor may also occur around the tendon, synovium, or joint capsule. Rare sites are the tongue, testis and liver. Chondroma of the fallopian tube is extremely rare. There are only two reports in the English literature. We present here the first reported case of extraskeletal chondroma of the fallopian tube causing transportation impairment of the fertilized ovum in a 32-year-old gravida 1, para 1 woman.

**43. Uterus didelphys with blind hemivagina and ipsilateral renal agenesis complicated by pyocolpos and presenting as acute abdomen, eleven years after menarche: our experience of a rare case with review of the literature.**

**M. Varras**, Ch. Akrivis, St. Karadaglis, G. Tsoukalos, Ch. Plis, I. Ladopoulos

[Clinical and Experimental Obstetrics and Gynaecology 35 \(2\):156-160, 2008.](#)

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

**Background:** Congenital anomaly of the Mullerian duct system can result in various urogenital anomalies including uterus didelphys with blind hemivagina and ipsilateral renal agenesis. The diagnosis of this condition is usually made after menarche, but its rarity and variable clinical pictures may contribute to a diagnostic delay for years after menarche. **Case:** A 24-year-old woman presented to the emergency room of the Department of Obstetrics and Gynecology complaining of severe worsening lower abdominal pain, vomiting and pus-like vaginal discharge. Physical examination revealed acute abdomen with diffuse lower abdominal tenderness, rebound and muscular resistance. Cervical and vaginal observation was impossible because of the discomfort of the patient. Bimanual gynecological examination showed high tenderness cervical motion. Transabdominal ultrasound scan was performed and the radiologist interpreted the ultraosonographic findings as existence of a pelvic mass with mixture appearance. The preoperative diagnosis was ruptured tubo-ovarian abscess and emergency laparotomy was performed. Free pus in the pelvis was found. Also, a double uterus with elongated and inflammatory right fallopian tube with pus passing out of its fimbrial end was observed. Vaginal examination under general anesthesia revealed an obstructed right hemivagina with vaginal pus-like discharge from a small fistula hole on the septate vagina. The final diagnosis was uterus didelphys with unilateral imperforate right hemivagina and pyocolpos. Transvaginal resection of the vaginal septum was performed and large amount of pus and blood was spilled out. Postoperatively, intravenous pyelography demonstrated agenesis of the right kidney. **Conclusion:** We demonstrated the

difficulty in correct diagnosis of this rare congenital anomaly of the female genital tract, especially after years from menarche. This condition should be considered to prevent misdiagnosis or suboptimal treatment and decrease morbidity and unnecessary surgical procedures.

**44. Emergency obstetric hysterectomy at two tertiary centers: a clinical analysis of 11 years experience**

**M. Varras**, Ch. Akrivis, Ch. Plis, G. Tsoukalos

**Clinical and Experimental Obstetrics and Gynaecology 2010, 37, 2:117-119.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

This was a retrospective clinical study of emergency hysterectomy, performed between 1997-2007 at two tertiary hospitals, to study incidence, indications and maternal mortality. We included any women who required emergency hysterectomy to control major postpartum haemorrhage after delivery, following a pregnancy of at least 24 weeks' gestation, regardless of the mode of delivery. There were 12 emergency hysterectomies, with a frequency of 0.0726% among 16,521 deliveries. Indications included uterine atony (4 cases), uterine rupture (3 cases), uterine retroversion (2 cases), abnormal placentation (2 cases) and amniotic fluid embolisation (1 case). The result was 2 maternal deaths. Although emergency obstetric hysterectomy is a life saving operation, it is associated with high maternal mortality.

**45. Antenatal sonographic diagnosis of pharyngeal teratoma: our experience of a rare case with review of the literature.**

**M. Varras**, Ch. Akrivis, Ch. Plis, G. Tsoukalos

**Obstetrics and Gynecology International 2009, Article ID 180643, 4 pages. An open access journal.**

<http://www.hindawi.com/journals/ogi/2009/180643.html>

**Abstract:**

**Background:** Teratomas are the most common tumors. They are usually localized in the sacrococcygeal area, while the pharyngeal localization is very rare. The number of cases of stomato-pharyngeal teratomas detected prenatally via sonography is very small. **Case Report:** We present the case of a 24-year-old primipara at 18 weeks' gestation, that at the routine ultrasound scan, the fetus was found with an echogenic mass, filling the stomato-pharyngeal cavity and protruding from the mouth. Other abnormalities were not found. Termination of pregnancy was achieved using misoprostol. A female stillborn fetus with a weight of 250 g and length of 25.5 cm was delivered. The postmortem and pathologic examination confirmed the diagnosis. **Conclusion:** Pharyngeal teratomas can be diagnosed with the use of ultrasounds *in utero* facilitating parents' counseling in early time.

**46. Misoprostol for second trimester abortion in women with prior uterine incision (EDITORIAL).**

**M. Varras**, Ch. Akrivis

**Clinical and Experimental Obstetrics and Gynaecology 2010, 37, 1:10-12.**

e-ISSN: 0390-6663

**IPP (Impact per Publication) (2015): 0.537**

**Abstract:**

Termination of pregnancy in the second trimester with misoprostol is safe and effective, but there is very limited published experience of its use in women with one or more previous cesarean sections. Uterine rupture might occur when misoprostol and oxytocin are used for pregnancy termination at the second trimester in women with previous uterine scars. In the English literature there are some case-series of studied women with a history of previous cesarean sections, in which misoprostol was used for second trimester termination of pregnancy. However, many different protocols have been used with different doses of misoprostol and different intervals between doses and it is difficult to draw definite conclusions. Therefore, the decision to attempt a pregnancy termination in the second trimester in cases with previous uterine scar should be made on a case-by-case basis, after consideration of number of previous cesarean sections and gestation age, and careful labor monitor of these patients.

**47. Spontaneous posterior uterine wall rupture at 37 weeks' gestation with history of suction curettage: our experience of a rare case with review of the literature**

**M. Varras**, Ch. Akrivis

**American Journal of Case Reports (e-ISSN 1941 – 5923) 2010; 11: 20-23.**

<http://www.amjcaserep.com>

**IPP (Impact per Publication) (2015): 0.601**

**Abstract:**

**Background:** Uterine perforation is an uncommon but serious life threatening event, and diagnosis is difficult in an unscarred gravid uterus. **Case:** A 44-year-old woman, gravida 5, para 2 with a history of two first trimester elective suction abortions presented at the 37th week of her gestation with spontaneous rupture of membranes. During labor induction with intravenous oxytocin, using a standard protocol, the woman had complained for sudden abdominal pain and profound fetal bradycardia had occurred. During the emergency laparotomy free blood in the abdomen was found and the fetus and the placenta were completely exteriorized from the uterus. A stillborn male infant weighing 3.400 g was removed from the abdomen. Also, the placenta was removed manually from the abdomen and the free blood was irrigated. The uterus was exteriorized for examination and a 7-cm longitudinal defect at the posterior surface of the uterus from the fundus to the supracervical area was identified as the source of rupture. A hysterectomy was performed because hemostasis was not achieved. **Conclusion:** Spontaneous uterine rupture is a rare but serious and catastrophic event. Sudden abdominal pain and fetal distress during active labor, in association with multigravidity should always prompt consideration of uterine rupture as a possible cause, in cases of unexplained anomalies in an unscarred gravid uterus. A history of possible myometrial damage should be taken in consideration as well.

#### **48. Uterocervical Prolapse during Pregnancy: a Case Report**

**M. Varras**

**American Journal of Case Reports (e-ISSN 1941 – 5923) 2010, 11 CR83-86.**

**Manuscript ID: 878551, <http://www.amjcaserep.com>**

**IPP (Impact per Publication) (2015): 0.601**

##### **Abstract:**

**Background:** The objective of reporting herein a case of uterocervical prolapse during pregnancy is to remind obstetricians of the complications and management of this problem during pregnancy. **Case Report:** A case of uterine prolapse is reported in a 31-year-old woman, gravida 3 para 2, which developed uterocervical prolapse during the third trimester of pregnancy. This case was managed conservatively and the patient had a normal delivery at term of a 3650 g male infant without fetal or maternal complications. Postnatally, the uterocervical prolapse recovered spontaneously. **Conclusions:** The diagnosis of uterine prolapse during pregnancy is very rare and frequent follow-up is necessary in order to prevent maternal and fetal complications. The successful management of the pregnancy should be individualized, but bed rest should be suggested in all pregnancies. Obstetricians should be familiar with this situation in pregnancy.

#### **49. Prenatal diagnosis of fetal hemivertebra: A case study with review of the literature**

**Varras M.,** Akrivis, Ch

**International Journal of General Medicine 2010, 3:197-201.**

**IPP (Impact per Publication) (2015): 1.302**

##### **Abstract:**

Hemivertebra is a rare congenital spinal malformation, where only one side of the vertebral body develops, resulting in deformation of the spine, such as scoliosis, lordosis or kyphosis. We present the ultrasonographic features of a fetus with hemivertebra at 20 weeks' gestation confirmed by postmortem radiography and pathological examination. Also, the prenatal literature is further reviewed. Useful background information is provided for both clinicians and other health professionals who are not familiar with this condition.

#### **50. Clinical, Ultrasonographic, Computed Tomography and Histopathological Manifestations of Ovarian Steroid Cell Tumor, Not Otherwise Specified: Our Experience of a Rare Case with Female Virilization and Review of the Literature**

**M. Varras,** Th. Vasilakaki, E. Skafida, Ch Akrivis

**Gynecological Endocrinology 2010, early on line 1-7.**

**IPP (Impact per Publication) (2015): 1.402**

##### **Abstract:**

**INTRODUCTION:** Ovarian steroid cell tumours, not otherwise specified (NOS) are rare sex cord-stromal tumours of the ovary. These tumours should be considered a cause of isosexual precocious puberty in children and virilisation in adults. **CASE:** We

report a case of 40-year-old woman with mental handicap who presented with 3 years of amenorrhea and progressive virilisation. Pelvic ultrasonography identified a 6.19 × 6.15 cm well-defined echogenic-multilobular mass arising from the left ovary. Fluid in the cul-de-sac was noted. Colour Doppler examination with endovaginal ultrasonography showed high vascularity of the tumour with low resistance to flow. A computed tomography (CT) scan of the upper and lower abdomen showed a lobular mass with diaphragms in the left adnexal structure and fluid in the cul-de-sac; no adrenal gland enlargement or additional tumour was detected. Laboratory analysis revealed increased levels of serum total testosterone. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Histological examination showed a benign steroid cell tumour, NOS without evidence of necrosis, haemorrhage or invasion. The immunohistochemical study showed that the tumour cells were positive for inhibin, CD 99, Melan A and vimentin and negative to CK AE1, CK AE3, progesterone and estrogen receptors. **CONCLUSION:** Careful medical history, physical examination, laboratory serum values and imaging studies are helpful in making the pre-operative diagnosis. Steroid cell tumours, NOS are usually benign, unilateral and characterised by the composition of two similar-appearing polygonal cell types. They differ from Leydig cell tumours in the lack of crystals of Reinke in their cytoplasm.

**51. Malignant Gastrointestinal Stromal Tumor Presenting with Hemoperitoneum in Puerperium: Report of a Case with Review of the Literature**

**Varras M.**, Vlachakos N., Vasilakaki Th., Akrivis Ch., Skafida E.

**World J Surg Oncol. 2010 Nov 7; 8(1): 95, doi:10.1186/1477-7819-8-95**

**IPP (Impact per Publication) (2015): 1.576**

**Abstract:**

**BACKGROUND:** Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors that develop in the wall of the gastrointestinal tract and their diagnosis during pregnancy or puerperium is extremely rare. **CASE:** A 28-year old patient presented with acute abdomen due to hemoperitoneum from a large mass arising of the small intestine with distended vessels on its top and a ruptured superficial vessel bleeding into the peritoneal cavity. The patient was at the tenth postpartum day of her first pregnancy. The preoperative diagnosis was a possible ovarian or uterine mass. After an emergency exploratory laparotomy a segmental bowel resection was performed, removing the tumor with a part of 3-cm of the small intestine. Histology revealed GIST with maximum diameter of 13 cm and mitotic rates more than 5 mitoses per 50 high power fields with some atypical forms, indicating a high risk malignancy. Immunohistochemical staining of the tumor tissue demonstrated strongly positive reactivity to CD 117 (c-kit) and CD34 in almost all the tumor cells. The patient was treated with oral imatinib mesylate (Gleevec) 400 mg daily for one year. Three years after surgery, the patient was alive without evidence of metastases or local recurrence. **CONCLUSION:** Considering that only few patients with gastrointestinal stromal tumors have been reported in the obstetrical and gynecological literature, the awareness of such an entity by the obstetricians-gynecologists is necessary in order to facilitate coordinated approach with the general surgeons and oncologists for the optimal care of the patients.

**52. Peritonitis due to iatrogenic colpotomy after Large Loop Excision of the Transformation Zone (LLETZ) in a Patient with Cervical Intraepithelial Neoplasia III: Our Experience of a Rare Case with Review of the Literature**

**Varras, M.,** Akrivis C., Anastasiadis A., Lekkas G., Diakakis G.

[European Journal of Gynaecological Oncology 33\(2\): 214-216.](#)

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

A case of peritonitis as an unusual complication of LLETZ (large loop excision of the transformation zone) for the treatment of CIN III associated with unrecognized iatrogenic posterior colpotomy is presented. After the procedure, the patient developed fever 38.3 degrees C and diffused severe pelvic pain. The contributing factors, prevention and management of this complication are discussed. Also, the complications of cold knife cervical conization and LLETZ procedure are reviewed.

**53. Expression of E-cadherin in human primary endometrial carcinomas: clinicopathological and immunohistochemical analysis of 30 cases.**

**Varras M.,** Skafida E., Vasilakaki T., Anastasiadis A., Vrachnis N., Akrivis C., Nikolopoulos G.

[European Journal of Gynaecological Oncology 2013;34\(1\):31-5.](#)

**IPP (Impact per Publication) (2015): 0.684**

**Abstract:**

**Introduction:** Decreased expression of E-cadherin has been associated with poorly differentiated endometrial carcinomas and poorer outcomes. **Aim:** It was to examine the distribution of E-cadherin immunohistochemical expression in specimens from

primary endometrial carcinomas and its relation to classical clinicopathological prognostic factors. **Material and methods:** Surgically resected tissues of 30 patients with primary endometrial carcinomas were studied. Histological type and grade, depth of myometrial invasion, lymph-vascular space invasion, fallopian tube or ovarian invasion, and presence of tumoral necrosis were evaluated. Immunohistochemical examination was performed on deparaffinized 4- $\mu$ m-thick sections. **Results:** The mean age of patients was 65 years old ( $\pm$  11.41). The 63.54% of carcinomas were moderately/poorly differentiated. No statistical correlation was found between the score or intensity of E-cadherin immunohistochemical staining (strong or moderate positive expression) and the clinicopathological factors tested. **Conclusions:** The association of E-cadherin immunoreactivity with the standard clinicopathological factors seems to be contradictory. The classical clinicopathological factors remain the most important prognostic parameters.

#### **54. Expression of antiapoptosis gene survivin in luteinized ovarian granulosa cells of women undergoing IVF or ICSI and embryo transfer: clinical correlations**

**Varras M.**, Polonifi K., Mantzourani M., Stefanidis K., Papadopoulos Z., Akrivis Ch., Antsaklis A.

**Reproductive Biology and Endocrinology 2012, 10:74; doi:10.1186/1477-7827-10-74.**

**IPP (Impact per Publication) (2015): 2.221**

#### **Abstract:**

**Background:** The purpose of the study was to determine the incidence of survivin gene expression in human granulosa cells during ovarian stimulation in Greek women with normal FSH levels, undergoing IVF or ICSI and to discover any correlation between levels of gene expression and clinical parameters, efficacy of ovulation or outcomes of assisted reproduction. **Methods:** Twenty nine women underwent ovulation induction for IVF or ICSI and ET with standard GnRH analogue-recombinant FSH protocol. Infertility causes were male and tubal factor. Cumulus-mature oocyte complexes were denuded and the granulosa cells were analyzed for each patient separately using quantitative reverse transcription polymerase chain reaction analysis for survivin gene expression with internal standard the ABL gene. **Results:** The ABL and survivin mRNA were detected in granulosa cells in 93.1%. The expression levels of survivin were significantly lower in normal women (male infertility factor) compared to women with tubal infertility factor ( $p = 0.007$ ). There was no additional statistically significant correlation between levels of survivin expression and estradiol levels or dosage of FSH for ovulation induction or number of dominant follicles aspirated or number of retrieved oocytes or embryo grade or clinical pregnancy rates respectively. **Conclusions:** High levels of survivin mRNA expression in luteinized granulosa cells in cases with tubal infertility seem to protect ovaries from follicular apoptosis. A subpopulation of patients with low levels of survivin mRNA in granulosa cells might benefit with ICSI treatment to bypass possible natural barriers of sperm-oocyte interactions.

#### **55. Markers of stem cells in human ovarian granulosa cells: is there a clinical significance in ART?**

Varras M, Griva T, Kalles V, Akrivis C, Paparisteidis N.

[Journal of Ovarian Research 2012 Nov 20;5\(1\):36; doi:10.1186/1757-2215-5-36.](#)

[IPP \(Impact per Publication\) \(2015\): 2.758](#)

**Abstract:**

**Background:** The purpose of the study was to determine the incidence of gene expression of Oct-4 and DAZL, which are typical markers for stem cells, in human granulosa cells during ovarian stimulation in women with normal FSH levels undergoing IVF or ICSI and to discover any clinical significance of such expression in ART. **Methods:** Twenty one women underwent ovulation induction for IVF or ICSI and ET with standard GnRH analogue-recombinant FSH protocol. Infertility causes were male and tubal factor. Cumulus–mature oocyte complexes were denuded separately and granulosa cells were analyzed for each patient separately using quantitative reverse-transcription–polymerase chain reaction analysis for Oct-4 and DAZL gene expression with G6PD gene as internal standard. **Results:** G6PD and OCT-4 mRNA was detected in the granulosa cells in 47.6% (10/21). The median of OCT-4 mRNA/G6PD mRNA was 1.75 with intra-quarteral range from 0.10 to 98.21. The OCT-4 mRNA expression was statistically significantly correlated with the number of oocytes retrieved; when the OCT-4 mRNA expression was higher, then more than six oocytes were retrieved ( $p=0.037$ , Wilcoxon rank-sum). No detection of DAZL mRNA was found in granulosa cells. There was no additional statistically significant correlation between the levels of OCT-4 expression and FSH basal levels or estradiol peak levels or dosage of FSH for ovulation induction. No association was found between the presence or absence of OCT-4 mRNA expression in granulosa cells and ovarian response to gonadotropin stimulation. Also, no influence on pregnancy was observed between the presence or absence of OCT-4 mRNA expression in granulosa cells or to its expression levels accordingly. **Conclusions:** Expression of OCT-4 mRNA, which is a typical stem cell marker and absence of expression of DAZL mRNA, which is a typical germ cell marker, suggest that a subpopulation of luteinized granulosa cells in healthy ovarian follicles (47.6%) consists of stem cells, which are not originated from primordial germ cells. Absence of Oct-4 gene expression in more than half of cases means probably the end of productive journey of these cells, towards the oocyte.

**56. Clinical and educational significance of case reports in medicine.**

Varras M. Editorial

[OA Case Reports 2012 Dec 21; 1\(1\):1.](#)

**Abstract:**

A case report describes unique aspects of a medical or surgical case and provides clear clinical and educational significance in medicine given its rapid contributions to the scientific literature and clinical practice. Despite the emphasis on randomized clinical trials, evidenced-based medicine, systemic reviews and meta-analyses, the case reports continue to provide a novel and exceptional knowledge in medical education. In this editorial, the clinical values of case reports in medicine and surgery are discussed and the details for the new journal *OA Case Report* are given. *OA Case Report* aims to develop the science of case reports and is committed to publish well-

written case reports from around the world in all the fields of basic medical sciences and clinical specialties and be a source of inspiration for clinicians and scientists about the newer research directions. *OA Case Reports* will publish research manuscripts dealing with a series of interesting medical and surgical cases, short communications and reports on all stages of the research process like hypothesis, methodology, study protocols and pilot studies. *OA Case Reports* encourages submissions about description of new knowledge, rare diseases or syndromes, new diagnostic tests, specific diagnostic images, rare clinicopathological correlations and surgical innovations as long as they are technically and scientifically correct.

### **57. The Expression of Genes in Human Ovarian Granulosa Cells during Assisted Reproduction Technologies and their Clinical Significance.**

**Varras M. Editorial**

**[Androl Gynecol: Curr Res 2012, 1:1.](#)**

#### **Abstract:**

Pre-ovulatory follicles contain two distinct types of granulosa cells which are the mural granulosa cells and the cumulus cells. At present, there are no morphological or physiological features of oocytes that can predict whether IVF fertilization will be successful, or whether is a need for ICSI unrelated to male factor infertility. Also, need for more accurate embryo selection in human assisted reproduction is needed to optimize and reduce the number of embryos transferred into the uterus reducing the risk of multiple gestations and maximizing the probability of pregnancy. In view of concept of all these and the need for independent prognostic markers of better outcomes in infertile patients undergoing IVF or ICSI, studies are focused on target genes in luteinized granulosa cells of the human ovaries. Apoptosis or survival of follicles dependent on autocrine and paracrine signals from theca cells, granulosa cells and oocyte. In the literature there is controversy about the clinical significance of the expression of apoptotic molecular factors in luteinized granulosa cells in infertile patients in cycles of IVF or ICSI, while promising signs give the estimation of survival factors for prognosis such as IGFs family and survivin.

### **58. Clinical Significance of Expression of Stem Cell Markers in Human Ovarian Luteinized Granulosa Cells during Assisted Reproduction Technologies**

**Varras M. Editorial**

**[Reproductive System & Sexual Disorders: Current Research, 2012, 1:e106, doi: 10.4172/2161-038X.1000e106](#)**

#### **Abstract:**

The adult human ovary is composed of various cell types. Preovulatory follicles contain two distinct types of granulosa cells that arise during folliculogenesis as the cell populations segregate upon formation of the fluid-filled follicular antrum. The granulosa cells line in the follicle wall, reside very close to the basement membrane and are essential for estrogen production and follicular rupture. The cumulus cells are closely connected to the oocyte through a gap junction network and are associated with the oocyte development. Paracrine interactions between ovarian somatic cells and germ cells are critical for normal follicular development and

oocytes also promote granulosa cell proliferation and differentiation. There are strong evidences that a subpopulation of granulosa ovarian cells have pluripotent and self-renewal capabilities. The presence of stem cell markers in the ovarian luteinized granulosa cells of women undergoing assisted reproduction technologies is an important subject for studies in terms of their possible regenerative role and theirs possible prognostic significance for the infertile citizens. Expression of the stem cell marker Oct-4 in human ovarian luteinized granulosa cells from women undergoing IVF or ICSI indicates the presence of stem cells in these cells. The absence of DAZL gene expression in these cells indicates that the stem cells found in granulosa cells cannot be differentiated in germ cells. Also, a clinical significance for the number of oocytes retrieved and the expression levels of Oct-4 in human luteinized ovarian granulosa cells is possible to exist. More specifically, the expression of Oct-4 mRNA in granulosa cells appears to play an important role in the regulation of follicular growth during assisted reproduction technologies.

#### **59. Osteoprotegerin as a marker of atherosclerosis in diabetic patients.**

Augoulea A, Vrachnis N, Lambrinouadaki I, Dafopoulos K, Iliodromiti Z, Daniilidis A, **Varras M**, Alexandrou A, Deligeoroglou E, Creatsas GC.

**International Journal of Endocrinology 2013, Article ID 182060, <http://dx.doi.org/10.1155/2013/182060>**

**IPP (Impact per Publication) (2015): 2.359**

#### **Abstract:**

Atherosclerosis is the principal cause of cardiovascular disease (CVD) and has many risk factors, among which is diabetes. Osteoprotegerin (OPG) is a soluble glycoprotein, involved in bone metabolism. OPG is also found in other tissues, and studies have shown that it is expressed in vascular smooth muscle cells. OPG has been implicated in various inflammations and also has been linked to diabetes mellitus. Increased serum OPG levels were found in patients with diabetes and poor glycemic control. Furthermore, prepubertal children with type 1 diabetes have significantly increased OPG levels. Receptor activator of nuclear factor kappa-B ligand (RANKL) is not found in the vasculature in normal conditions, but may appear in calcifying areas. OPG and RANKL are important regulators of mineral metabolism in both bone and vascular tissues. Few data are available on the relationship between plasma OPG/RANKL levels and endothelial dysfunction as assessed using noninvasive methods like ultrasound indexes, neither in the general population nor, more specifically, in diabetic patients. The aim of our review study was to investigate, based on the existing data, these interrelationships in order to identify a means of predicting, via noninvasive methods, later development of endothelial dysfunction and vascular complications in diabetic patients.

#### **60. Monocyte Function in the Fetus and the Preterm Neonate: Immaturity Combined with Functional Impairment**

Zoe Iliodromiti, Anastasis Anastasiadis, **Michail Varras**, Kalliopi I. Pappa, Charalambos Siristatidis, Vassilios Bakoulas, George Mastorakos, and Nikolaos Vrachnis

**Abstract:**

It is well known that the innate immunity system, involving the contribution of monocytes and macrophages, may dysfunction in fetuses and preterm neonates. Monocytes are capable of differentiating into dendritic cells (DCs) or into mucosal macrophages during certain infections and of producing inflammatory mediators such as TNF- $\alpha$  (tumor necrosis factor-alpha), nitric oxide, and reactive oxygen species. Fetuses as well as neonates are prone to infections as a result of a defective mechanism within the above mononuclear system. Monocyte function in fetuses and preterm neonates depends on the phagocytic and oxidative capacity of macrophages and their antigen-adhesion ability. Functional rather than anatomical impairment is probably the underlying cause, while a defective production of cytokines, such as TNF- $\alpha$ , IL-6 (Interleukin 6), IL-1 $\beta$  (Interleukin 1 beta), and G-CSF (Granulocyte Colony-Stimulating Factor), has also been involved. The insufficient production of the above inflammatory mediators and the phenomenon of endotoxin intolerance, which latter occurs during entry of any antigen into the premature neonate, place preterm neonates at higher risk for infections. Existing research data are herein presented which, however, are deficient and fragmental, this accounting for the fact that the precise pathophysiology of these disturbances is not yet fully clarified.

**61. Co-expression of Oct-4 and Survivin genes in human ovarian luteinized granulosa cell during in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) and embryo transfer programs.**

Varras M. Editorial

OA Case Reports 2013 Jan 31;2(1):1.

**Abstract:**

The adult human ovary is composed of various cell types. Pre-ovulatory follicles contain two distinct types of granulosa cells, which are the mural granulosa cells and the cumulus cells. Mural granulosa cells line the follicle wall and are responsible for oestrogen production and follicular rupture, while cumulus cells are closely connected to the oocyte through a gap junction network, which allows transfer of small molecules, glucose metabolites and ions and are responsible for the oocyte development. Paracrine interactions between theca cells, granulosa cells and oocyte are critical for normal follicular development. Apoptotic and survival factors take place during the interaction between the theca cells, granulosa cells and oocyte. Apoptotic factors inducing follicular atresia are GnRH, androgens, tumor suppressor protein P53, c-Myc, endothelins, protein bax, caspases, some members of the tumor necrosis factor family (TNF-alpha, Fas, FasL, TRAIL) and some members of the transforming growth factor-beta family (factor NODAL and AMH). Survival factors promoting follicular survival by FSH and LH include oestrogens, insulin and IGFs, growth hormone (GH), survivin, stem cell factor (SCF), kinase Akt, interleukin 1b (IL-1b), epidermal growth factor (EGF), member of the bcl-2 family, TGF-alpha, some

members of the TGF-beta family (activin, BMP-4, BMP-7 and growth differentiation factor-9), basic fibroblast growth factor (bFGF), KIT-ligand and c-KIT receptors. Analysis of prognostic biomarkers in follicular granulosa cells from ovaries during assisted reproduction technologies, for better reproductive outcomes seem to be a very intriguing approach. In a small sample of patients who underwent IVF or ICSI for tubal or male factor infertility (20 cases) we examined the co-expression of Oct-4 and Survivin in luteinized granulosa cells using Quantitative Competitive Real-Time PCR (QC RT-PCR) and found such event in 8 cases (8/20). Survivin mRNA was expressed in 19 cases (19/20), while Oct-4 mRNA was expressed in 9 cases (9/20). There was no statistically significantly correlation between the expression levels of Oct-4 and the expression levels of Survivin in luteinized granulosa cells during ART. We conclude that the low or high levels of mRNA Survivin gene expression are not directly related to the low or high levels of mRNA Oct-4 gene expression respectively in luteinized granulosa cells during ART.

### **62. Autoimmune oophoritis: Clinical presentation of an unusual clinical entity.**

**Varras M**, Anastasiadis A, Panelos J, Balassi E, Demou A, Akrivis CH.

[OA Case Reports 2013 Jan 31;2\(1\):7.](#)

#### **Abstract:**

**Introduction:** Autoimmune oophoritis is a rare condition, which provokes ovarian failure with either primary amenorrhea or secondary amenorrhea and a subsequent loss of fertility and ovarian hormonal function. The purpose of this study is to document the clinical findings from two patients with autoimmune oophoritis.

**Cases:** Two cases of autoimmune oophoritis are presented whose their histopathologic findings were consistent with the international literature. Both cases were histopathologically characterized by lymphocytic and plasmacytic inflammatory infiltrations around the cystic follicles. The inflammation was located both in theca and granular layer. **Conclusion:** Patients with autoimmune oophoritis should be recognized by the histopathology of the ovarian biopsies and these patients are at increased risk of developing other autoimmune disorders.

### **63. Extragenital Adenomatoid tumour of the omentum: An unusual location.**

Skafida E, Tsavari A, Koulia K, Myoteri D, Grammatoglou X, Zisi A, **Varras M**, Vasilakaki T.

[OA Case Reports 2013 Jan 31;2\(1\):4.](#)

#### **Abstract**

Adenomatoid tumors are benign mesothelial in origin neoplasms usually confined to the genital tract but have rarely been reported at other sites such as the omentum, pleura, heart, liver, adrenal gland, retroperitoneum and intestinal mesentery. We report a case of a 32 year old woman who presented to our hospital with a four days history of fever and pain in the right iliac fossa. Ultrasonography revealed a right ovarian cyst 2.5cm in diameter and fluid in douglaseio. A right partial oophorectomy was performed and during the operation a well circumscribed mass measured 2cm was observed in the omentum. Histological evaluation of the cyst showed features of

a cracked luteal cyst and the mass showed features of adenomatoid tumor. In the immunohistochemical study the lesional cells were positive for calretinin, D240,CK5/6,HMBE1,CKAE1,CKAE3 and calponin. Adenomatoid tumors are often found incidentally during surgical procedures. Tumors excision is therefore the treatment of choice.

**64. Prenatal diagnosis of a huge fetal immature sacrococcygeal teratoma: Our experience of a rare case and review of the literature.**

**Varras M**, Diakakis G, Monselas I, Akrivis CH.

**OA Case Reports 2013 Jan 31;2(1):10.**

**Abstract:**

**Purpose:** Sacrococcygeal teratomas are rare germ cell tumors associated with high perinatal and postnatal mortality and morbidity. The purpose of our study was to report a case of a fetal huge immature sacrococcygeal teratoma diagnosed prenatally and managed successfully in the early neonatal period with surgical resection of the tumor. **Case report:** A fetal mass with solid and cystic components in the sacral region of the fetus measuring 42X34-mm was detected during the fetal anatomy ultrasound scan, in a 28-year-old Greek woman, gravida 2, para 1. The fetal karyotyping showed normal number of chromosomes 13, 18 and 21 (46 XY). Polyhydramnios was seen, at 31 weeks of gestation and the patient was admitted to hospital owing to a risk of premature labor. Ultrasound examination showed the sacrococcygeal mass to be enlarged with maximum diameter of 20-cm. There were no signs of hydrops as demonstrated by the absence of ascites, pleural or pericardial effusion or placentomegaly. Color Doppler ultrasound examination showed extensive vascularization within the mass, suggesting increased blood flow into the tumor. Pulsed Doppler showed the resistance index (RI) of flow velocity waveforms on the tumoral arteries to be 0.51. Amnioreduction of 740-cc amniotic fluid was performed under ultrasonographic examination. Caesarean section was performed at 33 weeks' gestation due to profuse polyhydramnios via an upper vertical incision in the uterus. After the stabilization of the newborn, tumor resection was successfully performed on the first day after delivery. Grossly, in the surgical specimen the tumor measured 18-cm in its maximum diameter and weighted 1,500-g. **Conclusion:** Prenatal diagnosis and ultrasonographic follow-up are needed for the good prognosis of sacrococcygeal teratomas. Prenatal intervention should be considered when the fetus develops hydrops for fetal salvage or in cases with plactomegaly to ovoid the maternal risk of mirror syndrome.

**65. The awareness on sexual and reproductive health issues in urban and rural areas of Greece: a retrospective study on 200 adults 18-45 years old.**

Anastasiadis A, Koumousidis A, **Varras M**, Vrachnis N, Paltoglou G, Tzoumas N, Top L, Dimopoulos S, Deltsidou A, Salakos N.

**OA Women's Health 2013 Apr 01;1(1):2.**

**Abstract:**

Sexually transmitted diseases threaten every sexually active individual, whereas especially our younger adults, as more IT literate, should be better familiarized with

the various methods of STDs protection as well as of the traditional and modern contraception. Our purpose was to investigate and compare the awareness of 18-45 years old adults from urban and rural areas on sexual and reproductive health issues and to establish any potential new strategies for its best promotion. Two hundred individuals coming from either our capital, which represents the purest urban dimension of our Greek lifestyle spectrum, or one specific carefully selected, as a characteristic opposite non-urban dimension in our lifestyle scale, rural town, were stratified randomly and answered a three-part closed ended questionnaire. Useful results were extracted, like, for example, although 29.5% reported that they were in a committed relationship, trusted traditional methods of contraception and protection from STDs, like condom, 18% out of them has not been regularly using it. Moreover the percentage of hormonal contraception was low (9%). The younger the people and the more the urban lifestyle they have adopted, the lesser cautious on their choice of sexual partners are. Men still seem to be alternating between sexual partners and perform "one night stands" more frequently than women. Finally we came to the conclusion that the awareness on sex and reproduction is not so developed as we would expect from our adequate standard of living before the years of the economic crisis (<2010). We noticed many cases of fragmentary information, false view and high-risk sexual behavior. Moreover, mainland residents seem to be less informed about the current data of STDs and contraception, even though their behavior is less risky.

#### **66. The role of gynecologists in the years of demographic, political and economic crisis: the Greek aspect.**

Koumousidis A, **Varras M**, Tzoumas N, Top L, Boutas I, Sofoudis C, Katsetos C, Salakos N.

[OA Women's Health 2013 May 01;1\(1\):3.](#)

#### **Abstract:**

It is widely spread that History teaches the next generations, while every single generation contributes significantly to the enrichment of this valuable store of Knowledge. Greece is facing the epoch of political-economic declination; a fact with great impact on demographic parameters (mean lifeexpectancy, Malthusian parameter  $r$  of the Exponential Law in population dynamics, entropy-reproductive potential of population). **Objective:** To support the essential role of contemporary gynecologists against current demographic shrinkage. **Design & Methods:** We searched the web, looking for articles concerning history of nations and low birth rate. Historical proportionality was our main tool in selecting and distributing our results, as well as in extracting conclusions. Descriptive Statistics was applied, followed by sequence analysis, association rules, grouping and forecasting. Results: In Classical Sparta, the alarming decline of Spartan citizens, as commented on by Aristotle (384 BC – 322 BC), was one of the major factors, which led to the decline of the polis during the following Hellenistic and Roman Age. In his work on the rise of the Roman Republic and its gradual domination over Greece, Polybius (200-118 BC) cites the phenomenon of low birth rate, population decrease, subsequent agricultural decline and city desertion in Greece, attributing them to Fortune (Tyche). We studied that plagues and low birth rate among Roman citizens led to

depopulation in the Empire and in order this to be combated, barbarian tribes were actually welcomed into the Empire and encouraged to "set up shop" (as famous author and historian Will Durant states, 'An Empire is not conquered from without, until it has fallen from within'). On the other hand, several modern articles have attributed the EU economic crisis to low birth rate (ex. an article from the Head of Vatican bank, 2011). **Conclusions:** Historical proof of low birth rate leading as a factor to the catastrophe of a state is abundant. We, as gynecologists, could decelerate and maybe reverse this decline in births by informing properly our population on their fertility options, by combating the unnecessary abortions (by launching campaigns for parents, schools and media) and finally, by cultivating a positive attitude towards immigrants to Greece, as they can contribute significantly to the recovery of our wounded economy. Such actions may protect our nation from the Malthusian Catastrophe, as it was prophetically described by Thomas Malthus and published in the "An Essay on the Principle of Population" in 1798.

**67.** Petropoulou O, Koumousidis A, Katsetos C, **Varras M**, Katsoulis M. **Pathophysiologic and hormonal changes affecting pain during pregnancy: A review.**

[OA Women's Health 2013 Jun 01;1\(1\):5.](#)

**Abstract:**

There are significant pathophysiologic and hormonal changes that take place during pregnancy, which affect almost every system in the body and contribute to successfully overcoming the challenges of pregnancy and labour. The changes noted in the first trimester of pregnancy are mainly of hormonal etiology, considering the fact that progesterone, estrogens, human chorionic gonadotrophin, prostaglandins and endorphins are significantly increased.

**68.** Koumousidis A, **Varras M**, Sofoudis C, Salakos N.

**Evaluation of breast cancer occurrence in patients with previous IVF treatment.**

[OA Women's Health 2013 Jun 01;1\(1\):8.](#)

**Abstract:**

**Introduction:** Breast cancer affects mostly 50-69 years old women, with history of previous breast or colon cancer, subfertility, nulliparity, ionising radiation, late menopause, smoking, fatty diet and positive for malignancies family history. Researchers support the multiple, unsuccessful under IVF treatment, efforts to be an etiologic factor for the disease. **Objective:** To evaluate the breast cancer's occurrence in correlation to previous IVF exposure for the treatment of subfertility. **Material and methods:** We searched the web using several keywords, such as "ART/IVF/breast cancer/malignancies/BRCA 1-2 mutations", and found lots of interesting articles, forums, blogs and case reports. All this data-warehouse became a very useful tool in our hands in order to proceed in the basic Online Analytical Processing during data-mining of 86 breast cancer "web-cases" surgically treated at least seven years after their last IVF treatment (association rules, sequence analysis, classification, clustering and forecasting regarding the type of the tumor (benign,

malignant), the number of the previous IVF treatments and several involving in breast cancer factors (age, obesity, parity, history of ovarian, breast or colon cancer, smoking)). **Results:** Low cancer risk was found after IVF treatment in some studies, while other researchers observed higher malignancy rate in IVFpatients comparing to the risk in the general population. Several studies attributed the increased risk to the underlined pathology causing both the infertility and the malignancy, while several other scientific efforts are focused on findings proving higher rates for malignant tumors in the ART-treated patients. We noticed that this controversy is attributed to the lack of a systematic and worldwide-accepted classification in the cancer patients, who have undergone IVF treatment(s), in terms of several factors: age, body-weight, parity, previous breastfeeding, habits and positive for malignancies history. Studies on these factors and their coactions in the malignant breast behavior after IVF exposure should proceed any data-processing in order the latter to become scientifically fertile. **Conclusions:** If we classify the IVF-candidate women in terms of their personal and family history, we will find a way out of this controversy and eventually, minimize the various potential long-term breast malignant complications in IVF treatment through adequately informing our general population.

**69.** Kalles V, Papapanagiotou I, Mariolis-Sapsakos T, **Varras M.**

**Presence of brain metastases in patients with ovarian cancer: a place for BRCA1/2 gene testing?**

**OA Case Reports 2013 Aug 08;2(7):62.**

**Abstract:**

Ovarian cancer represents the fourth most common female cancer, with the presence of brain metastases being rare (<2%) among these patients. This percentage, although, has risen in the last decades, possibly due to the improved anticancer therapies that result in better survival of these patients. A literature review that was conducted revealed several cases of ovarian cancer patients with brain metastasis being positive for BRCA1/2 gene mutations. In ovarian cancer, BRCA1/2 mutations are associated with different survival and disease – free survival, while the development of brain metastases has been thought to represent a different biologic phenotype of the disease. Therefore, in this communication, we discuss the basis of the hypothesis that ovarian cancer patients with brain metastases should be screened for BRCA1/2 gene mutations.

**70. Varras M,** Anastasiadis A, Akrivis C, Gialelis J. **Pentalogy of Cantrell in the human fetuses: A rare congenital malformation. OA Case Reports 2013 Nov 15;2(15):143.**

**Abstract:**

**Introduction:** Pentalogy of Cantrell consists of the following five congenital major malformations: (a) a defect in the anterior diaphragm, (b) a midline supraumbilical anterior abdominal wall defect, (c) a defect in the diaphragmatic pericardium, (d) various congenital cardiovascular malformations and (e) a defect in the lower part of the sternum typically with ectopia cordis. Moreover, additional features may exist to a various extent. The pathogenesis of pentalogy of Cantrell remains uncertain and

most of the cases are thought to be sporadic. Genetic and environmental factors or disrupted defects of the vessels have also been implicated. Prenatal diagnosis of pentalogy of Cantrell is easily obtained when malformations such as ectopia cordis with omphalocele or other midline abdominal wall defects are visible during the foetal ultrasound scans. The diagnosis of pentalogy of Cantrell with ultrasonography is made after the 12th week of gestation, because of the normal bowel herniation outside the abdomen before that time and offers the option of termination of the pregnancy in cases with complexity of the cardiac defects and serious associated malformations. With the Color and Power Doppler ultrasound scans the heart is easily recognized protruding outside the thorax. Also, MRI enhances the visualization of the defects, confirms the diagnosis and guides the surgical decisions. In patients choosing to continue the pregnancy the best treatment approach includes a multispecialty medical team and the surgical corrections should be attempted at the same time soon after delivery. The aim of this review is to remind in Obstetricians Gynaecologist the rare entity of pentalogy of Cantrell. **Conclusion:** The pentalogy of Cantrell is an extremely rare entity with a generally poor prognosis. The treatment of all the congenital heart defects found in this entity is very important for the long-term prognosis of children.

#### **(ii). Posters on-line**

**Poster number:** 376

**Title:** Expression of E-cadherin in Human Primary Endometrial Carcinomas: Clinicopathological and Immunohistochemical Analysis of 30 cases  
**MICHAEL VARRAS**, Evangelia Skafida; Thivi Vasilakaki; Anastasis Anastasiadis; Christodoulos Akrivis; Zacharias Papadopoulos; Nikolaos Vrachnis; Georgios Nikolopoulos

[http://www.postersessiononline.com/173580348\\_eu/congresos/20figo/aula/-Mon\\_376\\_20figo.pdf](http://www.postersessiononline.com/173580348_eu/congresos/20figo/aula/-Mon_376_20figo.pdf)

**Poster number:** 10

**Title:** Oct-4 gene expression and absence of DAZL gene expression in luteinized ovarian granulosa cells of women undergoing IVF or ICSI and embryo transfer

**MICHAEL VARRAS**, Konstantinos Stefanidis; Theodora Griva; Vasileios Kalles; Zacharias Papadopoulos; Christodoulos Akrivis; Depy Mavrogianni ; Dimitris Loutradis

[http://www.postersessiononline.com/173580348\\_eu/congresos/20figo/aula/-Mon\\_10\\_20figo.pdf](http://www.postersessiononline.com/173580348_eu/congresos/20figo/aula/-Mon_10_20figo.pdf)

#### **(iii). SCIENTIFIC WORKS PUBLISHED IN INTERNATIONAL JOURNALS AS PROCEEDINGS OF INTERNATIONAL CONFERENCES**

##### **1. ras oncogene activation in endometrial carcinomas.**

**Varras M.N.**, Koffa M., Ergazaki M., Koumantakis E., Michalas S., Aravantinos D., Spandidos D.A.

**Publication:** International Journal of Oncology 1995, 7(Suppl): p998.

**Proceedings of the "1st World Congress on advances in Oncology, Hotel Complex "Aster Palace", October 22-26, Vouliagmeni, Athens, Greece".**

**IPP (Impact per Publication) (2015): 3.019**

**2. Elevated binding of glyccorticoid receptors to H-*ras* GRE in human endometrial and ovarian tumors as compared to adjacent normal tissue.**

Zachos G., Zoumpoulis V., **Varras M.**, Sekeris C.E., Spandidos D.A.

**Publication:** [Biochemical and Biophysics Newsletter 1996, 40:p40-p41.](#)

[Proceedings of the "44<sup>th</sup> Scientific Conference of the Hellenic Biochemical and Biophysical Society, January 12-13, 1996, Athens, Greece"](#)

**3. The association of the H-*ras* oncogene and steroid hormone receptors in gynecological cancer.**

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Publication:** [Clinical & Experimental Metastasis 1996, 14 \(Suppl 1\): p27.](#)

[Proceedings of the "Sixth International Congress of the Metastasis Research Society, 8-11 September 1996, Aula of the University Gent, Belgium"](#)

**IPP (Impact per Publication) (2015): 2.851**

**4. Activation of H-*ras* oncogenic potential in human endometrial and ovarian tumors by specific steroid receptor binding in H-*ras* DNA elements.**

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Congress:** [Oncology 1996 International Conference on Experimental and Clinical Oncology, October 3-5, 1996, Island of Kos, Greece.](#)

**Publication:** [International Journal of Oncology 1996, 9\(Suppl\): p845.](#)

[Proceedings of the "Oncology 1996 International Conference on Experimental and Clinical Oncology, October 3-5, 1996, Island of Kos, Greece"](#)

**IPP (Impact per Publication) (2015): 3.019**

**5. Detection of *ras*-gene mutation in human ovarian tumors of Greek patients.**

**Varras M.N.**, Sourvinos G., Flouris G., Diakomanolis E., Lekka-Katsouli I., Michalas S., Spandidos D.A.

**Congress:** [XV FIGO World Congress of Gynaecology and Obstetrics, August 3-8, 1997, Copenhagen.](#)

**Publication:** [Acta Obstetricia et Gynecologica Scandinavica 1997, 76 \(Suppl\): p37.](#)

[Proceedings of the XV FIGO World Congress of Gynaecology and Obstetrics, August 3-8, 1997, Copenhagen](#)

**IPP (Impact per Publication) (2015): 2.074**

**6. Altered binding of p53 wild-type and mutant forms to the H-*ras* element in human endometrial and ovarian tumor, as compared to their respective normal tissue.**

Zachos G., **Varras M.N.**, Michalas S., Spandidos D.A.

**Publication:** [Acta Obstetricia et Gynecologica Scandinavica 1997, 76 \(Suppl\): p37.](#)

[Proceedings of the XV FIGO World Congress of Gynaecology and Obstetrics, August 3-8, 1997, Copenhagen](#)

**IPP (Impact per Publication) (2015): 2.074**

**7. Altered binding of p53 protein to the H-ras 1 element in human endometrial and ovarian tumors.**

Zachos G., **Varras M.N.**, Michalakis S., Spandidos D.A.

**Publication:** [International Journal of Oncology 1997, 11 \(Suppl\):p906.](#)

[Proceedings of the 2nd World Congress on Advances in Oncology, October 16-18, 1997, Athens](#)

**IPP (Impact per Publication) (2015): 3.019**

**8. Emergency obstetrics hysterectomy in two tertiary centers: A clinical analysis of 11 years experience (No. 189).**

**Varras M.**, Akrivis C., Karadaglis S., Kanellopoulos N., Antoniou N., Ladopoulos I.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280. Proceedings of the XXI European Congress on Perinatal Medicine, 2008, page 75.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Purpose:** Emergency obstetric hysterectomy is a life saving procedure. Purpose of the study was to present frequency, indications and possible complications related to emergency postpartum hysterectomy. **Methods:** In this retrospective clinical study, performed between 1997-2007 at the maternity units of "TZANEIO" General Hospital of Piraeus and "HATZIKOSTA" Hospital of Ioannina Greece, we studied all the cases of emergency peripartum hysterectomies to control major postpartum hemorrhage after delivery, following a pregnancy of at least 24 week's gestation regardless of the mode of delivery. **Results:** During the study period there were 16,521 deliveries and 5,360 were by cesarean section. In this period, 12 emergency hysterectomies were performed, with a frequency of 0.0726%; 7 emergency hysterectomies were performed after cesarean section and 5 after normal labor (including vaginal assisted delivery with the use of vacuum). Between the 7 cases after cesarean section, the 4 were after previous cesarean section; 4 of the women were primiparas and 8 multiparas. Abnormal vaginal bleeding was the reason in all of the cases. Indications included uterine atony (4 cases), uterine rupture (3 cases), uterine retroversion (2 cases), abnormal placentation (2 cases) and amniotic fluid embolisation (1 case). The result was 2 maternal deaths and 3 stillborns. No bladder lesions occurred. **Conclusion:** Peripartum emergency hysterectomy is an urgent procedure with high risk of blood loss during the operation. The gynecologists should be well trained to perform the operation and taking the on-time decision for the surgical operation can prevent serious complications.

**9. Disruption of prior uterine incision during second trimester abortion with misoprostol in a woman with previous cesarean section (No. 190).**

**Varras M.**, Akrivis C., Karadaglis S., Plis C., Tsoukalos G., Ladopoulos I.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280. Proceedings of the XXI European Congress on Perinatal Medicine, 2008, page 75.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Background:** Few cases with uterine rupture during the second trimester abortion with misoprostol and a previous uterine scar have been reported in the literature.

**Case:** A 23-year-old woman with a prior low transverse cesarean section presented at 22 weeks' gestation for pregnancy termination because of multiple fetal abnormalities. She was given 800 microg misoprostol intravaginally every 4 h until regular contractions began. After the third dose she had vaginal bleeding and severe uterine contractions. She aborted completely 2 h later the last dose. Under general anesthesia, uterine rupture was diagnosed at site of the previous cesarean section. A laparotomy revealed a 7-cm anterior uterine wall rupture at the site of the previous cesarean section with considerable hemorrhage into the abdominal cavity. The uterus was repaired. **Conclusion:** Misoprostol use in the second trimester in a woman with previous cesarean section can lead to uterine rupture.

**10. Spontaneous posterior uterine wall rupture at 37 weeks' gestation with history of suction curettage: our experience of a rare case with review of the literature (No. 227).**

Akrivis C., **Varras M.**, Tsoukalos G., Karadaglis S., Ladopoulos I., Antoniou N.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280.](#)

[Proceedings of the XXI European Congress on Perinatal Medicine, 2008, page 85.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Background:** Uterine perforation or uterine wall defect is an uncommon but serious complication of elective abortion or evacuation of placental parts retained in the uterine cavity during the puerperium. The most hazardous problem of uterine perforation is uterine rupture during a subsequent pregnancy, which can be fatal for both fetus and mother. **Case:** A 44-year-old woman, gravida 5, para 2 with a history of two elective suction abortions presented at 37 weeks with spontaneous rupture of membranes. During labor induction with oxytocin the woman complained for sudden abdominal pain and profound fetal bradycardia occurred. During the emergency laparotomy there was free blood in the abdomen, and the fetus and the placenta were completely exteriorized from the uterus. A stillborn male infant weighing 3,400 g was removed from the abdomen. Also, the placenta was removed manually from the abdomen and the free blood was irrigated. The uterus was exteriorized for examination and a 7-cm longitudinal defect in the posterior surface of the uterus from the fundus to the supracervical area was identified as the source of rupture. The edges of the defect were without bleeding suggesting a chronic process. However, a hysterectomy was performed because hemostasis was not achieved. **Conclusion:** Spontaneous uterine rupture is a rare but serious and catastrophic event. Sudden abdominal pain and fetal distress after previous trauma to the uterus from prior suction abortion should always prompt consideration of uterine rupture as a possible cause.

**11. Uterine prolapse during pregnancy (No. 229).**

**Varras M.**, Akrivis C., Karadaglis S., Plis C., Tsoukalos G., Ladopoulos I.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280.](#)

[Proceedings of the XXI European Congress on Perinatal Medicine, 2008, pages 85-86.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Introduction:** Uterine prolapse is very rare during pregnancy. It can be associated with maternal discomfort, cervical desiccation and ulceration, urinary tract infection, acute urinal retention, spontaneous abortion and preterm labour. We present a case of uterine prolapse, which was managed successfully during pregnancy and labor.

**Case:** A 31-year-old woman, gravida 3, para 2, presented in the antenatal outpatient clinic at 32 weeks of gestation complaining of something coming out from her vagina. The patient had no medical history. She experienced the same symptoms during her previous pregnancy that disappeared postpartum. Physical examination revealed an elongated cervix, with moderate edema, but without ulcerations. The cervical os was closed. The patient was managed conservatively with bed rest and evaluation every 2 weeks. During the course of pregnancy, the cervix has been further elongated. At 39 weeks of gestation, she was admitted to the hospital with spontaneous onset of labor and a cervical dilatation of 5 cm. She gave birth to a male of 3,650 g. Her postpartum course was satisfactory and she discharged from hospital on day 3. The follow up after 3 months revealed complete resolution of uterine prolapse. **Conclusion:** The diagnosis of uterine prolapse during pregnancy and frequent follow-ups are necessary in order to prevent maternal and fetal complications. The successful management of the pregnancy should be individualized but bed rest should be suggested at all pregnancies.

**12. Prenatal diagnosis of fetal hemivertebra (No 228).**

**Varras M.,** Akrivis C., Karadaglis S., Plis C., Ladopoulos I., Antoniou N.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280.](#)

[Proceedings of the XXI European Congress on Perinatal Medicine, 2008, pages 101-102.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Introduction:** Hemivertebra is a rare congenital malformation of the spine, where only one side of the vertebral body develops, leading to deformation of the spine, such as scoliosis, lordosis, or kyphosis. **Case:** We present the ultrasonographic findings of a fetus with solitary hemivertebra diagnosed at 20 weeks' gestation. The triple test at 16 weeks' of gestation was negative: AFP 42 ng/ml (MoM = 0.992), E3 3.8 nmol/l (Mom = 1.834), free beta-hCG 28 ng/ml (MoM = 2.806). The ultrasound scan at 16 weeks' gestation showed no malformations. At the b-level ultrasound scan at 20 weeks' gestation the biparietal diameter was 46 mm, the abdominal circumference 145 mm, the fetal femur length 32 mm and the possible fetal weight 348 g. Amniotic fluid was at normal limits. However, a distortion at the lubar legion of the spine, at the longitudinal plane was demonstrated. A small triangular bony structure was wedged against the normal vertebral bodies. No other abnormalities

were detected. The initial diagnosis was single hemivertebra and the parents decided to terminate the gestation. The labour was induced using misoprostol and the ultrasonographic findings were confirmed with a simple x-ray of the stillbirth fetus and with pathologic examination. **Conclusion:** The characteristic US findings of hemivertebra help at the early detection of this situation in order the parents to have on time information to make a decision to proceed or not with their gestation.

**13. Prenatal diagnosis of congenital cystic adenomatoid malformation of the fetal lung (No.306).**

**Varras M.**, Akrivis C., Karadaglis S., Plis C., Tsoukalos G., Ladopoulos I.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280.](#)

[Proceedings of the XXI European Congress on Perinatal Medicine, 2008, page 107.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Introduction:** Congenital cystic adenomatoid malformation of the fetal lung is an extremely rare developmental abnormality characterized by an excessive overgrowth of the terminal respiratory bronchioles at the expense of the saccular spaces. Sonography is important for the prenatal diagnosis. We report the diagnosis of a congenital cystic malformation of the lung in utero and present the ultrasonographic findings and the postmortem pathology of this entity. **Case:** A 33-year-old primipara was presented for routine ultrasonographic examination at 20 weeks' gestation; congenital adenomatoid malformation of the fetal lungs, type II, was diagnosed. On the right side of the chest an area with a maximum diameter of 18.5 mm and with small cystic lesions was recognized. The maximum diameter of the cysts was found to be 0.5 cm. There were no fetal ascites, mediastinum shift, pericardial effusion, pleural effusion, congenital diaphragmatic hernia or other fetal abnormalities. The couple decided to terminate the pregnancy, which was carried out using misoprostol. A female fetus was delivered, weighting 330 g. The postmortem examination showed a congenital cystic adenomatoid malformation of the right middle lobe of the lung, which was histologically classified as type II. No other congenital abnormalities were found. Pathologically, the cysts had the appearance of bronchiolus-like structures and were lined with cuboidal and focally columnar epithelium; distended alveoli were present. The airways were normal in structure. The fetal karyotype was 46, XX. **Conclusion:** We describe the ultrasound and pathologic findings of a rare case of congenital cystic adenomatoid malformation of fetal lung-type II.

**14. Prenatal diagnosis of fetal hemivertebra (No. 329).**

**Varras M.**, Akrivis C., Karadaglis S., Plis C., Tsoukalos G., Ladopoulos I.

**Publication:** [Journal of Maternal-Fetal and Neonatal Medicine Jan 2008, Vol. 21, No. s1, Pages 21-280: 21-280.](#)

[Proceedings of the XXI European Congress on Perinatal Medicine, 2008, page 113.](#)

**IPP (Impact per Publication) (2015): 1.424**

**Abstract:**

**Introduction:** Teratomas are the most common tumors. They are usually localized in the sacrococcygeal area, while the pharyngeal localization is very rare. The number of cases of stomato-pharyngeal teratomas detected prenatally via sonography is very small. **Case:** We present the case of a 24-year-old primipara at 18 weeks' gestation, that at the routine ultrasound scan, the fetus was found with a echogenic mass, filling the stomato-pharyngeal cavity and protruding from the mouth. Other abnormalities were not found. Termination of pregnancy was achieved using misoprostol. A female stillborn fetus with a weight of 250 g and length of 25.5 cm was delivered. The postmortem and pathologic examination confirmed the diagnosis. **Conclusion:** Pharyngeal teratomas can be diagnosed with the use of ultrasounds in utero in order to terminate the pregnancy in early time.

**15. Survivin gene expression levels in luteinized ovarian granulosa cells of women undergoing IVF or ICSI and embryo transfer: clinical correlations (No. 175).**

**Varras, M.,** Polonifi A., Mantzourani M., Mavrogianni D., Stefanidis K., Griva T., Bletsas R., Dinopoulou V., Drakakis P., Loutradis D.

**Publication:** [Human Reproduction 2012, 27 \(suppl.2\): ii162-ii205. doi: 10.1093/humrep/27.s2.77.](#)

[Proceedings of the 28<sup>th</sup> ESHRE Annual Meeting, Turkey, 1-4 July 2012.](#)

**IPP (Impact per Publication) (2015): 4.343**

**Abstract:**

**Introduction:** The objective of the study was to determine the incidence of expression of SURVIVIN in human granulosa cells during ovarian stimulation in women with normal FSH levels, undergoing IVF or ICSI. To test if the levels of genes expression in granulosa cells could indicate number of oocytes retrieved, oocyte quality and developmental competence. To discover any correlation of gene expression with the clinical parameters of patients, the efficacy of ovulation and the outcome of IVF or ICSI. To explore if the examined gene could be a molecular prognostic marker for embryo development to increase the chance of a successful pregnancy with assisted reproductive technologies by optimizing oocyte and embryo selection. **Material and Methods:** All of the patients were stimulated with standard GnRH analogue-recombinant FSH protocol. Total RNA was extracted from granulosa cells and was reverse transcribed into cDNA using specific designed primers for SURVIVIN. SURVIVIN mRNA in human granulosa cells was detected by RT-PCR using fluorescent probes. To determine the steady amount for SURVIVIN mRNA levels in granulosa cells, a quantitative competitive PCR (QC RT-PCR) was developed. The number of transcripts of studied target genes was normalized according to the number of transcripts of the internal standard genes ABL. The respective quantitative ratio was determined by the density of the target to the internal standard: Survivin mRNA / ABL mRNA. **Main Outcome Measure(s):** The expression rates of SURVIVIN of granulosa cells surrounding the oocytes were determined in the studied patients. Many variables were analyzed: age, BMI, infertility causes, infertility duration, previous IVF/ICSI cycles, serum concentrations of FSH, LH, progesterone, AMH at the beginning of the menstrual cycle, serum PRL levels, as measured during one of the previous six months, serum 17 $\beta$ -estradiol levels on the 5th day of FSH treatment and on the day of hCG, duration of stimulation, total FSH dose used for ovarian

stimulation, ovarian response, oocyte maturity, embryo quality (grade), good quality embryos score, fertilization and pregnancy rates. **Results:** ABL and SURVIVIN mRNA was detected in the granulosa cells in 93.1% (27/29). The median of SURVIVIN mRNA /ABL mRNA was 0.45 with intra-quarteral range from 0.22 to 2.94. The quantitative ratio of Survivin mRNA was significantly lower in normal women (male infertility factor) compared to women with tubal infertility factor ( $p = 0.007$ , Wilcoxon rank-sum test). There was no additional statistically significant correlation between the levels of SURVIVIN expression and the estradiol levels or the dosage of FSH for ovulation induction or the number of dominant follicles aspirated or the clinical pregnancy rates respectively. There was no statistically significant correlation between the levels of SURVIVIN expression and the number of retrieved oocytes. **Conclusions:** High levels of SURVIVIN mRNA expression in luteinized granulosa cells in cases with tubal infertility seems to be observed for possible protection from follicular apoptosis. A subpopulation of patients with low levels of SURVIVIN mRNA in granulosa cells might benefit with ICSI treatment to bypass possible natural barriers of the sperm-oocyte interactions.

#### (iv). SCIENTIFIC WORKS PUBLISHED AS COMPLETE PAPERS IN GREEK JOURNALS

##### 1. [The role of androgens in the regulation of ovarian function] [in Greek].

Varras M., Michalakis S.

**Adolescent Gynecology Reproduction and Menopause 1995, 7, 31-39.**

##### Abstract:

The androgens experimentally seem to have some local action on the ovaries which depends on the concentration and type of androgen which is used in the trial, the conditions in the culture medium and the development stage of the follicle. In hyperandrogenism there is an abnormal steroidogenic mechanism in the ovaries. Hyperandrogenism is accompanied by hyperinsulinaemia which stimulates steroidogenesis acting in the IFG receptors. In hyperandrogenism, it is proved that insulin induces the increased production of androgens in the ovaries, the exercise and diet probably help in the treatment. In polycystic ovarian syndrome (PCOS) the levels of free circulation testosterone are increased resulting atresia of the follicles as a primary or secondary event. Treatment of PCOS includes the improvement of hirsutism, the induction of ovulation and the reduction of weight.

##### 2. [Activation of K-ras gene in tumors of the endometrium] [in Greek].

Varras M., Koffa M., Koumantakis E., Protopappa E., Ergazaki M., Spandidos D.

**Greek Obstetrics and Gynecology 1995, 7, 51-56.**

##### Abstract:

In this study we examined 62 cases of endometrial adenocarcinomas, 15 cases of normal and 4 cases of hyperplastic endometrium, for the presence of point mutations in codon 12 of the K-ras gene. The polymerase chain reaction (PCR) technique was used to amplify a 157 bp region, followed by restriction fragment length polymorphism (RFLP) analysis to identify the point mutations. Eight out of 62 tumors (13%) were found to carry a K-ras codon 12 point mutation and the presence

of mutation was associated only with the histologic type. It is suggested that the mutational activation of *K-ras* gene may be involved in the early stages of the development of a small percentage of endometrial tumors.

**3. [Endometrial cancer: molecular, biochemical and clinical correlations]** [in Greek].

Diakomanolis E., **Varras M.N.**

**Gynecological Oncology and Colposcopy 1996, 2, 169-177.**

**Abstract:**

Recent studies have begun to elucidate the molecular events involved in the development and biological behavior of endometrial carcinoma. First, it has been shown that some endometrial neoplasms show alterations in several oncogenes and tumor suppressor genes including *ras*, *c-myc*, *c-erb-2*, *fms* and *p53*. In addition, it has been shown that endometrial neoplasms often have augmented production of growth factors and epidermal growth factor receptor. Moreover, with multivariate analysis, DNA ploidy was found to be a useful prognostic indicator of persistent or recurrent disease. Finally, long-term administration of tamoxifen as adjuvant therapy for breast cancer has been associated with an increased incidence of endometrial carcinoma. Understanding the mechanisms involved in endometrial malignancy development and growth will allow design better therapeutic strategies. More objective and reproducible prognostic variables and tumor markers will improve the predictiveness of prognosis.

**4. [Preimplantation diagnosis of genetic abnormalities]** [in Greek].

**Varras M.N.**

**Adolescent Gynecology Reproduction and Menopause 1997, 9, 116-127.**

**Abstract:**

Although healthy babies, having been born after preimplantation diagnosis for genetic diseases, this technique is still in experimental phase. A variety of strategies have been developed, which include polar body biopsy, removal of cells from multicell stage embryos, and biopsy of the trophoctoderm from expanded blastocysts. The prospect of preimplantation diagnosis of genetic disorders requires the development of highly sensitive genetic tests which can be performed on small numbers of cells removed from a preimplantation stage embryo. The diagnostic techniques include chromosomal analysis, biochemical assays, polymerase chain reaction (PCR) and in situ hybridization. All these aspects of the procedures are considered in this review.

**5. [Primary squamous cell carcinoma of the endometrium: a case report and review of the literature]** [in Greek].

**Varras M.N.,** Kioses E., Diakomanolis E., Papaspyrou R., Sotiropoulou M., Deligeoroglou E., Koukoulomatis P., Michalas S.

**Adolescent Gynecology Reproduction and Menopause 1997, 9, 311-316.**

**Abstract:**

Primary squamous cell carcinoma of the endometrium is very rare, with only 64 cases reported in the medical literatures since 1892. We report a new case of squamous cell carcinoma of the endometrium. In situ hybridization was performed to determine the presence of human papillomavirus (HPV) in the tumor of this case. HPV was not detected. Additionally, the aetiology, the clinical aspects and the treatment of the primary squamous cell carcinoma of the corpus uteri are discussed.

**6. [Molecular approach of ovarian cancer] [in Greek].**

Koumantakis E., **Varras M.N.**

**Adolescent Gynecology Reproduction and Menopause 1997, 9, 222-230.**

**Abstract:**

Despite the fact that ovarian cancer is the leading cause of death from gynecologic cancer, we know little about its molecular pathology. It has been described that some sporadic ovarian cancers exhibit activation of several proto-oncogenes (*ras*, *erbB-2*, *myc*, *fms*, *bcl-2*) and inactivation of tumor suppressor genes, such as p53 and BRCA1. The majority of familial ovarian cancers are due to mutations of the tumor suppressor gene BRCA1. Also, it seems that the *H-ras* oncogene is implicated in carcinogenesis of ovarian cancer because of its abnormal regulation by the steroid hormones or the tumor suppressor protein P53. The discovery of the mechanisms of resistance to chemotherapy can lead to the design of new therapeutic strategies, while in the future the gene therapy could reduce the mortality and morbidity of women with ovarian cancer.

**7. [Finding foreign bodies in the vagina of a young girl] [in Greek].**

Deligeoroglou E., Charalambidis V., **Varras M.**, Panitsa-Fafli Ch., Creatsas G.

**Adolescent Gynecology Reproduction and Menopause 1998, 10, 228-230.**

**Abstract:**

Insertion of foreign objects in the vagina of young girls is the cause of recurrent uncured (persistent) vaginitis. We present a case of finding a plastic ruler 0.5X6 cm and 18 hair pins in the vagina of an 11-year-old girl with a bifid hymen and bloody vaginal discharge of unknown etiology for 1 year. The main diagnostic method was hymenoscopia.

**(v) SCIENTIFIC WORKS PUBLISHED IN GREEK JOURNALS AS PROCEEDINGS OF GREEK CONFERENCES.**

**1. [Involvement of ras oncogene in the pathogenesis of endometrial cancer] [in Greek].**

**Varras M.**, Koffa M., Koumantakis E., Ergazaki M., Protopappa, Sfiniadakis I., Spandidos D.A.

**Presentation:** 1<sup>st</sup> Congress of the Greek Society of Colposcopy and Cervical Pathology

**Publication:** **Gynecological Oncology and Colposcopy 1995, 1, 77.**

**Abstract:**

Endometrial cancer is considered to arise as a consequence of genetic alterations of proto-oncogenes and tumor-suppressor genes, which alter progressively benign endometrium in less differentiated histologically lesions. Clinical involvement of activated *K-ras* oncogenes in tumorigenesis of endometrial adenocarcinoma has been described, whereas the incidence of point mutations in the H-or *N-ras* genes is not yet known. This study examined sixty-one (61) cases of endometrial adenocarcinomas preserved in paraffin, for the presence of point mutations at codon 12 of the *K-ras* gene, H-and *N-ras*. For this purpose the technique of polymerase chain reaction (PCR) and RFLP analysis were used. Eight of the 61 samples (13%) were found to have a mutation at codon 12 of the gene *K-ras*, and only 4 samples (7%) was found to have a mutation at codon 12 of the gene *H-ras*. Mutations were not detected for the gene *N-ras*. The postoperative status of the patients was known in 51 cases with a mean follow-up duration of 35 months. Three out of the 12 (25%) patients with *K-ras* or *H-ras* mutation and eight of the 39 (21%) patients without mutation died. The statistical analysis of the findings showed correlation (Kruskall-Wallis test,  $K^* = 16.20$ ,  $p = 0.011$ ) between the presence of mutations at codon 12 of *K-ras* gene and the histological type of adenocarcinoma of the endometrium. Also correlation (Fischer's Exact test,  $p = 0.021$ ) was found between the presence of mutations at codon 12 of *H-ras* gene and the stage at FIGO. In conclusion, the presence of activated *ras* oncogene is a relatively common (20%) genetic abnormality, which is involved in carcinogenesis of endometrial cancer in Greece. Activation of *H-ras* gene appears to occur late in the carcinogenicity of endometrium and also it is shown that the causative agents of endometrial cancer are associated with the histological type of the disease.

#### **(v). PRESENTATIONS IN INTERNATIONAL CONFERENCES**

##### **1. Detection of *ras* gene mutations in endometrial carcinomas.**

**Varras M.**, Koffa M., Ergazaki M., Koumantakis E., Ergazaki M., Spandidos D.A.

**1st European Medical Students' Symposium, April 15-16, 1995, Athens;** final programme-abstracts page 35.

##### **Abstract:**

Endometrial carcinoma is thought to arise from a serious of somatic mutations which alter benign endometrium to progressively less differentiated histological lesions. One genetic alteration implicated in the endometrial carcinogenesis is the mutational activation of the *ras* genes. Recent studies have revealed *K-ras* mutations at codon 12 in 10-37% of endometrial tumors, as well as in 6-16% of endometrial hyperplasias, suggesting that a *ras* mutation may be one of the earliest oncogenic events in endometrial cancer. H- and *N-ras* gene point mutations have been detected at a lower rate. Although *ras* gene mutations are apparently present in some endometrial tumors, their incidence is still unclear, and little is known regarding their possible clinical significance. This is of particular interest because of the continuing need to improve current methods of predicting risk of recurrence in gynecological neoplasia. In this study we examined 62 cases of endometrial adenocarcinomas, 15 cases of normal and 5 cases of hyperplastic endometrium, for the presence of point mutations in codon 12 of the *K-* and *H-ras* genes. The

polymerase chain reaction (PCR) technique was used, followed by restriction fragment length polymorphism (RFLP) analysis to identify the point mutations. Eight out of the 62 tumors (13%) were found to carry a *K-ras* codon mutation, while no mutations were found for the *H-ras* gene. The presence of *K-ras* mutation was associated only with the histological type of the tumor. It is suggested that the mutational activation of *K-ras* gene may be involved in the early stages of the development of a small percentage of endometrial tumors.

## **2. *ras* oncogene activation in endometrial carcinomas.**

**Varras M.N.**, Koffa M., Ergazaki M., Koumantakis E., Michalas S., Aravantinos D., Spandidos D.A.

**1st World Congress on Advances in Oncology, Hotel Complex "Aster Palace", October 22-26, Vouliagmeni, Athens, Greece; [International Journal of Oncology 1995, 7 \(Suppl\): p998.](#)**

### **Abstract:**

Endometrial carcinoma is thought to arise from genetic alterations of proto-oncogenes and tumor suppressor genes, which alter benign endometrium to progressively less differentiated histological lesions. Implications of *K-ras* activation have been reported, while the frequency of *H-* or *N-ras* gene mutations is still unclear. In this study we examined 55 formalin-fixed, paraffin-embedded tissues of primary endometrial carcinomas, 4 endometrial hyperplasias and 28 specimens of normal endometrium, for the presence of codon 12 point mutations in *K-*, *H-* and *N-ras* genes. The polymerase chain reaction (PCR) technique was used, followed by restriction fragment length polymorphism (RFLP) analysis to identify the point mutations. Codon 12 point mutations of the *K-ras* gene were detected in 8 out of 55 cases (14.5%), while only 4 (7.3%) were found positive for the *H-ras* codon 12 point mutation. Mutations of the *N-ras* gene were not detected. No correlation was found between the presence of *K-ras* or *H-ras* gene mutations and the clinicopathological parameters, as well as the survival of the patients determined by Kaplan-Meier curves and log rank analysis. The only association found statistically significant was between *H-ras* gene mutations and FIGO stage of the tumor (Fisher's exact test,  $p=0.011$ ). These results indicate a possible role of activated *ras* genes in a subset of endometrial carcinomas.

## **3. Elevated binding of glucocorticoid receptors to *H-ras* GRE in human endometrial and ovarian tumors as compared to adjacent normal tissue.**

Zachos G., Zoumpourlis V., **Varras M.**, Sekeris C.E., Spandidos D.A.

**44th Scientific Conference of the Hellenic Biochemical and Biophysical Society, January 12-13, 1996, Athens; [Biochemistry and Biophysics Newsletter 1996, 40: p40-p41.](#)**

### **Abstract:**

Glucocorticoids regulate transcription of a number of genes by the direct interaction of the hormone receptor complex with specific DNA binding sites, also known as glucocorticoid response elements (GREs). In a previous study we identified a potent GRE at the first intron of the *H-ras1* proto-oncogene (1). *H-ras* gene is involved in

multiple signal transduction pathways under normal cellular growth (2) and is implicated in many types of human tumors, both through mutation (3) and overexpression (4). Hormonal steroids are considered to be tumor promoters (5). The cooperation between glucocorticoid hormones and the T24*ras* H-*ras* gene in hormonal promotion of human tumors through abnormal hormonal regulation. Indications correlating the levels of hormone receptors and prognosis of the disease, survival and response to hormonal therapy are also provided (7,8) In this study, radiolabelled oligonucleotides encompassing H-*ras* GRE were used in gel retardation assays, together with nuclear extracts from human endometrial and ovarian lesions and from adjacent normal tissue. We found increased binding of the glucocorticoid receptor to these oligonucleotides in 10/11 endometrial and 7/7 ovarian tumors, as compared to the corresponding normal tissues. These results suggest a role of elevated hormonal levels in endometrial and ovarian neoplasia. Moreover, expression of the H-*ras* gene is elevated in breast tumors (9). Our results also imply that elevated expression of H-*ras* occurs through hormonal regulation in genital tumors, thus suggesting a role of H-*ras* overexpression in human tumorigenesis.

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9. Spandidos D.A., Agnantis N.J. Anticancer Res. 1984, 4, 269-272.

### 4. The association of the H-*ras* oncogene and steroid hormone receptors in gynecological cancer.

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Sixth International Congress of the Metastasis Research Society, 8-11 September 1996, Aula of the University Gent, Belgium; [Clinical and Experimental Metastasis 1996, 14 \(Suppl 1\): p27.](#)**

### Abstract:

The ras family of cellular oncogenes is one of the most frequently detected families of transformation – including genes in human solid tumors. Overexpression of the *ras* oncogene product is associated with tumorigenicity, invasiveness and metastatic potential in a variety of human carcinomas, such as lung, gastric, head and neck, cervical and breast tumors. Additionally, H-*ras* cooperates with glucocorticoids in cell transformation and ovarian hormones in the development of mammary carcinomas in rats. Steroid hormone receptors control gene expression as hormone – activated

transcriptional activators, by specifically binding to palindromic DNA sequences, called hormone response elements (HREs). Steroids are considered to be tumor promoters and steroid levels influence the cure rates and survival of the patients with gynecological tumors. Transcriptional activation of nuclear proto-oncogenes, such as *c-fos*, *c-jun*, *c-myc*, provides an example to better understand the cell cycle control by steroids. In a previous study, we showed that the human *H-ras* gene contains within its first and fourth introns sequences that are specifically recognized by HeLa extract-derived glucocorticoid and estrogen receptors, respectively [1]. We then used gel retardation assays to compare the level of steroid receptor binding in *H-ras* elements, using nuclear extracts from human endometrial and ovarian lesions and from the adjacent normal tissue. We found elevated glucocorticoid receptor binding in 90% of endometrial and in all ovarian tumors versus normal tissues tested. Elevated estrogen receptor binding was found in all ovarian tumors tested. We therefore suggest that the *H-ras* proto-oncogene is directly implicated in human gynecological cancer through abnormal hormone regulation and that steroid receptor DNA binding levels may be of prognostic significance in hormonally responsive human cancers. **Reference: 1.** Zachos G. et al. *Int. J. Oncol.* 1995, 6, 595-600.

#### **5. Activation of H-ras oncogenic potential in human endometrial and ovarian tumors by specific steroid receptor binding in H-ras DNA elements.**

Zachos G., **Varras M.**, Koffa M., Ergazaki M., Spandidos D.A.

**Oncology 1996 International Conference on Experimental and Clinical Oncology, October 3-5, 1996, Island of Kos, Greece; [International Journal of Oncology 1996, 9 \(Suppl\) p845.](#)**

#### **Abstract:**

Steroid hormone receptors differentially control the transcription of target genes by binding to palindromic DNA elements, referred to as hormone response elements (HREs). Hormonal steroids are also considered to be tumor promoters. We have previously reported that the human *c-H-ras* proto-oncogene contains within its first and fourth introns sequences that specifically bind the glucocorticoid (GRE) and estrogen (ERE) receptor molecules, respectively – Zachos et al (*Int. J. Oncol.* 1995, 6, 595-600). In the present study, we examined in gel retardation assays, the level of receptor binding in *H-ras* elements, using nuclear extracts derived from human endometrial and ovarian lesions, compared to the adjacent normal tissue. We found increased binding of the glucocorticoid receptor to the *H-ras* GRE in more than 90% of endometrial and in all ovarian tumors tested, as compared to the corresponding adjacent normal tissue. Furthermore, we found elevated binding of the estrogen receptor in *H-ras* ERE in all pairs of ovarian tumor/normal tissue tested, whereas in ER negative control breast tumor/normal tissue pairs, no differences in ER DNA binding levels were observed. These results suggest that *H-ras* oncogenic potential is directly activated in gynecological, hormonally-responsive human tumors by specific steroid receptor binding in *H-ras* DNA elements.

#### **6. Ras-oncogene mutations in human ovarian tumors.**

Flouris G.A., Sourvinos G., **Varras M.N.**, Spandidos D.A.

**3rd European Medical Students' Symposium, Scientific Association of Greek Medical Students, Capsis Palace Conference Centre, 11-13 Aprile 1997, Heraklion Crete, Greece; Book of abstracts, page 48.**

**Abstract:**

*K-ras* codon 12 mutations in epithelial ovarian neoplasms show a wide range between 4-32% in invasive carcinomas and 20-48% in borderline tumors. However, the difference in the incidence and prevalence of *ras* gene mutations in epithelial ovarian neoplasms from patients of different ethnic populations and geographic regions, need to be established clearly. In our study we used PCR-RFLP analysis to show the pattern of point mutations in codon 12 of *K-ras*, *H-ras*, *N-ras* genes in 80 tissue specimens of Greek patients with epithelial ovarian tumors. *K-ras* and *H-ras* gene mutations were detected in 11/54 (20%) and 3/54 (5.55%) cases with primary invasive epithelial ovarian carcinomas respectively, while *N-ras* gene mutations were not found. No mutation of *K*-, *H*- and *N-ras* genes were detected in 23 ovarian cystadenomas. In one out of three borderline ovarian tumors (33%) we found an *H-ras* gene mutation. The prevalence of mutations in *K-ras* gene was 1/11 (9%) in mucinous, 7/27 (26%) in serous, ½ (50%) in endometrioid and 2/7 (29%) in clear cell adenocarcinomas and in the *H-ras* gene 1/11 (9%) in mucinous and 2/27 (7.4%) in serous adenocarcinomas. We found no statistical correlation between the presence of *ras* gene mutations and the histologic subtypes. Our data suggest that *ras* gene activation in epithelial ovarian carcinomas occur in a small subset of Greek patients and is not associated with the differentiation of the epithelial cells.

**7. Detection of *ras*-gene mutation in human ovarian tumors of Greek patients.**

**Varras M.N.**, Sourvinos G., Flouris G., Diakomanolis E., Lekka-Katsouli I., Michalas S., Spandidos D.A.

**XV FIGO World Congress of Gynaecology and Obstetrics, August 3-8, 1997, Copenhagen; [Acta Obstetricia et Gynecologica Scandinavica 1997, 76 \(Suppl\): p37.](#)**

**Abstract:**

In epithelial ovarian neoplasms *K-ras* codon 12 mutations show a wide range between 4-32% in invasive carcinomas and 20-48% in borderline tumors. The difference in the incidence and prevalence of *ras* gene mutation in epithelial ovarian neoplasms from patients of different geographic regions and ethnic populations, however, needs to be established clearly. In this study, we showed the pattern of point mutations in codon 12 of the *K-ras*, *H-ras*, *N-ras* genes, using PCR-RFLP analysis in 80 tissue specimens of Greek patients with epithelial ovarian tumors. *K-ras* and *H-ras* gene mutations were detected in 11/54 (20%) and 3/54 (5.55%) cases with primary invasive epithelial ovarian carcinomas, respectively, while *N-ras* gene mutations were not found. No mutations of *K*-, *H*- and *N-ras* genes were detected in 23 ovarian cystadenomas. In one out of the three borderline ovarian tumors (33%) we found an *H-ras* gene mutation. The prevalence of mutations in *K-ras* gene was 1/11 (9%) in mucinous, 7/27 (26%) in serous, ½ (50%) in endometrioid and 2/7 (29%) in clear cell adenocarcinomas, and in *H-ras* gene 1/11 (9%) in mucinous, and 2/27 (7.4%) in serous adenocarcinomas. No statistical correlation was found between the presence of *ras* gene mutations and the histologic subtypes. Our present study

suggests that ras gene activation in epithelial ovarian carcinomas occur in a small subset of Greek patients and is not associated with the differentiation of the epithelial cells.

**8. Alterating binding of p53 wild-type and mutant forms to the H-ras element in human endometrial and ovarian tumor, as compared to their respective normal tissue.**

Zachos G., **Varras M.**, Michalakis S., Spandidos D.A.

**XV FIGO World Congress of Gynaecology and Obstetrics, August 3-8, 1997, Copenhagen; *Acta Obstetrica et Gynecologica Scandinavica* 1997, 76 (Suppl): p37.**

**Abstract:**

The P53 protein functions as a trans-acting transcriptional factor controlling the expression of genes important in transcription, DNA synthesis and repair, cell differentiation and apoptosis. The ras family of cellular oncogenes is one of the most frequently detected families of transformation – inducing genes in human tumors. We found that human c-H-ras1 gene contains within its first intron a p53 element, which functions as a transcriptional enhancer. Using nuclear extracts from human endometrial and ovarian tumors and from adjacent normal tissues in gel retardation assays, we found altered binding of the P53 protein to the H-ras p53 element in tumors and from adjacent normal tissues in gel retardation assays, we found altered P53 binding in the tumor tissue in 5/11 (45%) pairs tested, thus suggesting overexpression of the wild-type P53, P53 mutated forms that bind DNA. In 3/11 (27%) cases, no P53 binding was detected, indicating P53 mutated forms that fail to bind DNA. Concerning ovarian tumors, we found elevated binding in tumor versus normal tissue in 2/5 (40%) pairs tested, no differences in P53 binding levels in 2/5 (40%) and no P53 binding in tumor tissue in 1/5 (20%) of cases. These experimental results suggest a direct implication of the H-ras gene in the development of human tumors, through abnormal regulation by the P53 protein.

**9. Altered binding of p53 protein to the H-ras 1 element in human endometrial and ovarian tumors.**

Zachos G., **Varras M.N.**, Michalakis S., Spandidos D.A.

**2nd World Congress on Advances in Oncology, October 16-18, 1997; *International Journal of Oncology* 1997, 11 (Suppl): p906.**

**Abstract:**

The P53 protein functions as a trans-acting transcription factor controlling the expression of genes important in transcription, DNA synthesis and repair, cell differentiation and apoptosis. The ras family of cellular oncogenes is one of the most frequently detected families of transformation – inducing genes in human tumors. We found that human c-H-ras1 gene contains within its first intron a p53 element, which functions as a transcriptional enhancer. Using nuclear extract from human endometrial and ovarian tumors and from adjacent normal tissues in gel retardation assays, we found altered binding of the P53 protein to the H-ras p53 element in tumor versus normal tissue. Concerning endometrial tumors, we found elevated P53 binding in the tumor tissue in 5/11 (45%) pairs tested, thus suggesting

overexpression of the wild-type P53, or P53 mutated forms that bind DNA. Concerning ovarian tumors, we found elevated binding in tumor versus normal tissue in 2/5 (40%) pairs tested, no differences in P53 binding levels in 2/5 (40%) and no P53 binding in tumor tissue in 1/5 (20%) of cases. These experimental results suggest a direct implication of the H-ras gene in the development of genital tumors, through abnormal regulation by the P53 protein status (wild-type or mutated) will provide a better understanding of the mechanisms of tumorigenesis relating to gene regulation by P53 protein.

#### **10. Intraperitoneal bupivacaine irrigation for the reduction of postoperative pain following operative gynaecological laparoscopy.**

**Varras M.**, Miskry T., Katsetos Ch., Magos A.

##### **Ανακοίνωση:**

**a>. Annual Scientific Meeting of the British Society for Gynaecological Endoscopy, 21-22 May 1999, Plymouth, U.K.**

**b>. 8th Congress of the European Society for Gynaecological Endoscopy, 16-18 September 1999, Stockholm, Sweden; Book of Abstracts P1:24.**

##### **Abstract:**

**Aim:** Installation of intraperitoneal local anaesthesia during diagnostic laparoscopy and laparoscopic sterilization has been shown to reduce postoperative pain. However, the value of this technique in laparoscopic surgery with a greater degree of dissection or manipulation of viscera is unclear. To evaluate this we have designed a prospective trial to determine the place of intraperitoneal irrigation with the long acting local anaesthetic, bupivacaine. **Methods:** All women scheduled to have operative laparoscopy for gynaecological disease were eligible with exception of patients with heart disease or known hypersensitivity to bupivacaine. A pain tolerance questionnaire was completed prior to admission. All patients had a standard general anaesthetic and intra- and post-operative analgesic protocol. 10 ml of 0.5% bupivacaine was injected at the port sites prior to any incisions being made. At the completion of surgery, 500 ml of N/Saline containing 10 ml 0.5% bupivacaine was instilled into the peritoneal cavity. The patients were asked to complete a visual analogue pain scale in the recovery room immediately following surgery, and at 4 and 24 hours postoperatively. A note was made of the use of parental or oral analgesics during this time. **Results:** The study is on-going and our results will be presented at the meeting. If our results are favourable, we plan to carry out a prospective placebo controlled randomised trial in to the use of intraperitoneal bupivacaine for the management of post-operative pain after laparoscopic surgery. **Conclusions:** Intraperitoneal instillation of long-acting local anaesthetics may further reduce the trauma of laparoscopic surgery and make it even more acceptable as a day-case surgery.

#### **11. Laparoscopic excision of ovarian dermoid cyst in a bag.**

**Varras M.**, Miskry T., Magos A.

**8th Congress of the European Society for Gynaecological Endoscopy, 16-18 September 1999, Stockholm, Sweden; Book of Abstracts V1:1.**

**12. Torsion of the uterine adnexa: A clinical and pathological study.**

**Varras M.**, Antoniou S., Bassiotou V., Georgakila S., Paissios P.

**The fifth Athens Congress on woman's Health & Disease. Gynecologic & Reproductive Issues, Athens (Greece) 26-29/09/2002; Adolescent Gynecology Reproduction and Menopause 2002, 14(3): page 250.** Official Journal of the Hellenic Society of Pediatric and Adolescent Gynecology.

**13. Clinicopathological study of a case with primary small-cell carcinoma of the endometrium.**

**Varras M.**, Akrivis Ch., Ntemou A., Hadjopoulos G., Stefanaki S., Antoniou N.

**The fifth Athens Congress on woman's Health & Disease. Gynecologic & Reproductive Issues, Athens (Greece) 26-29/09/2002; Adolescent Gynecology Reproduction and Menopause 2002, 14(3): page 276.** Official Journal of the Hellenic Society of Pediatric and Adolescent Gynecology.

**Abstract:**

**Introduction:** Small-cell carcinomas are almost always primary in the lungs and are highly malignant. These tumors may also occur in the female genital tract. However, primary small-cell carcinoma of the endometrium is extremely rare with very few cases reported in the English literature. This tumor may exhibit evidence of neuroendocrine differentiation and has a high propensity for systematic spread and poor prognosis. **Case:** A 55-year-old postmenopausal woman with primary small-cell carcinoma of the endometrium, FIGO stage Ib, underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and sampling node biopsies of the parametrial spaces, followed by adjuvant combined chemotherapy. **Conclusion:** A case of small-cell carcinoma of the endometrium, is reported and its clinical, histological and immunohistological features are discussed.

**14. Intraoperative haemorrhage secondary to perforation of uterine fibroid after cystic degeneration: Unusual CT findings resembling malignant pelvic tumor.**

**Varras M.**, Antoniou S., Samara Ch., Frakala S. Angelidou-Manika Z. Paissios P.

**The fifth Athens Congress on woman's Health & Disease. Gynecologic & Reproductive Issues, Athens (Greece) 26-29/09/2002; Adolescent Gynecology Reproduction and Menopause 2002, 14(3): page 285.** Official Journal of the Hellenic Society of Pediatric and Adolescent Gynecology.

**Abstract:**

**Introduction:** Uterine leiomyomas are benign tumors of uterine smooth muscle resulting from the proliferation of myometrial cell hypersensitive to oestrogens. These tumors are the most common pelvic neoplasms in women in 20% to 30% of women aged 30 years and over. Patients may present with abnormal uterine bleeding, pelvic pressure or pain, urinary symptoms, spontaneous abortion, poor obstetrical outcome and infertility depending on the lesion size and location. However, intraperitoneal haemorrhage is an extremely rare complication of myomatous uterus. **Case:** A 37-year-old white nullipara presented in the emergency room with acute, lower-abdominal pain, which reportedly started after riding over a bump on a motorcycle. On examination, the abdomen was diffusely tender, with

moderate spasm and rebound tenderness in both iliac fossae. Pregnancy test was negative. Computed tomography revealed a soft-tissue mass with cystic components and inhomogeneous appearance. Free fluid in the peritoneal cavity suggested ascites. The patient underwent an exploratory laparotomy. A ruptured, actively bleeding, subserosal, nonpedunculated, cystic degenerated uterine fibroid was found, as well as approximately two liters of free, bloodstained peritoneal fluid and clots. Subtotal hysterectomy without salpingo-oophorectomy was performed, followed by evacuation of fluid and clots. The patient's postoperative course was uneventful. **Conclusion:** Definitive, preoperative diagnosis of perforated haemorrhaging uterine fibroid is difficult. Exploratory laparotomy is both diagnostic and therapeutic in this rare life threatening condition.

**15. Mucinous cystadenoma of the ovary with hyperplasia of Leydig cells during pregnancy.**

Antoniou N., **Varras M.**, Akrivis Ch., Stefanaki S.

The fifth Athens Congress on woman's Health & Disease. Gynecologic & Reproductive Issues, Athens (Greece) 26-29/09/2002; [Adolescent Gynecology Reproduction and Menopause 2002, 14\(3\): page 288](#). Official Journal of the Hellenic Society of Pediatric and Adolescent Gynecology.

**16. Prerupture ultrasonographic diagnosis of interstitial pregnancy in the first trimester of pregnancy: A case report and review of the literature.**

Akrivis Ch., **Varras M.**, Kyparis J., Demou A., Stefanaki S., Antoniou N.

The fifth Athens Congress on woman's Health & Disease. Gynecologic & Reproductive Issues, Athens (Greece) 26-29/09/2002; [Adolescent Gynecology Reproduction and Menopause 2002, 14\(3\): page 294](#). Official Journal of the Hellenic Society of Pediatric and Adolescent Gynecology.

**Abstract:**

**Introduction:** Interstitial ectopic pregnancy is an infrequent type of ectopic pregnancy, occurring in 2% to 4% of all extrauterine pregnancies. It is a life-threatening condition because rupture tends to occur in the second trimester of pregnancy resulting in profuse bleeding. The correct diagnosis requires awareness of this condition. The purpose of this study is to present the sonographic picture of an unruptured interstitial pregnancy diagnosed in the first trimester of pregnancy. **Case:** A 33-year-old, gravida 4, para 3 woman admitted at the department of Obstetrics and Gynaecology, "G. Chatzikosta" General State Hospital of Ioannina, after having eight weeks of amenorrhea. The urine pregnancy test was positive. A transvaginal ultrasound examination revealed an eccentrically located gestational sac surrounded by a thin myometrial layer and a separate empty uterine cavity with endometrial echoes. The fetus had positive cardiac activity and a crown-rump length of 9mm corresponding to a gestational age of about 8 weeks. This ultrasonographic picture was suggestive of an interstitial pregnancy. A subsequent Doppler flow evaluation revealed an increased blood flow to that area, consistent with the diagnosis. Quantitative serum beta-hCG level was reported as 20,100mIU/mL. The levels of serum progesterone were 32.5nmol/L. Conrual resection was performed by laparotomy. The postoperative course of the patient was unremarkable. **Conclusion:**

The postoperative course of the patient was unremarkable. **Conclusion:** The preoperative diagnosis of an unruptured interstitial pregnancy is difficult. The sensitive beta-hCG assays and the transvaginal ultrasonography are the principle tools used to make the diagnosis. Herein we presented a new case of interstitial pregnancy emphasizing its ultrasonographic findings. Also, the histopathology is described and the international literature reviewed.

**17. Primary mucinous carcinoma of the sigmoid colon metastatic to the wall of a benign ovarian dermoid cyst: A case report and review of the literature.**

Tsimogiannis E., Akrivis Ch., **Varras M.**, Antoniou N., Kitsiou E., Stefanaki S.

**5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p122**

**Abstract:**

**Introduction:** Primary colon carcinoma metastatic to benign ovarian tumors is an extremely rare event. The very unusual case of metastatic disease in the wall of an ovarian dermoid cyst is reported. **Case:** A 64-year-old patient underwent a sigmoidoscopy because of bleeding through the rectum. The biopsies confirmed the presence of an adenocarcinoma of the colon. After routine for colectomy preoperative preparation, an exploratory laparotomy through a supra-subumbilical midline incision was performed. A mass in the sigmoid colon and a large right ovarian tumor were found. Bilateral salpingo-oophorectomy and radical resection as for carcinoma of the sigmoid colon following by an end-to-end anastomosis were successfully performed. The excised bowel and adnexa were sent for pathologic examination. The patient received routine postoperative care. The excised colon was 23 cm in length and an ulceration measuring 9.5 X 5-cm was found. The size of the right ovary was 12 X 8 X 4-cm. Twenty-nine lymph nodes were found in the mesocolon. Light microscopy showed the presence of a well-differentiated mucinous adenocarcinoma of the colon, which invaded the submucosa, the muscularis propria, the subserosa and the pericolic tissues. Seventeen out of the twenty-three regional nodes were positive for metastatic disease. A dermoid cyst was found in the right ovary with extensive invasion of its wall by a mucinous adenocarcinoma. In the wall of the cyst, skin appendages and residues of thyroid tissue were seen. The tubes and the left ovary were free of disease. **Conclusion:** The final diagnosis was primary mucin-producing adenocarcinoma of the sigmoid colon. The metastasis of mucinous colon carcinoma in the wall of benign ovarian tumor was an incidental finding, which in cases like this might lead to misinterpretation as a primary ovarian neoplasm. The histological findings are presented and the international literature is reviewed.

**18. Prematal diagnosis of congenital cystic adenomatoid lung malformation: A case report and review of the literature.**

Akrivis Ch., **Varras M.**, Demou A., Bellou A., S. Stefanaki S., Antoniou N.

**5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p117.**

**19. Aggressive angiomyxoma of the vulva: A case report and review of the literature.**

Akrivis Ch., **Varras M.**, Lekkou P., Kitsiou E., S. Stefanaki S., Antoniou N.  
**5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p91.**

**Abstract:**

**Introduction:** Aggressive angiomyxoma is a distinctive, extremely uncommon, soft tissue tumor, which is predominantly found in the female pelvis and perineum. It occurs almost exclusively in women of reproductive age. Also, it rarely occurs in men with reported involvement of the scrotum, inguinal region, spermatic cords and pelvis. This tumor is characterized by its locally infiltrative behavior due to incomplete surgical excision. **Case:** A 28-year-old woman developed an aggressive angiomyxoma of the left vulva. Physical examination disclosed a soft, non-tender mass within the left labium minus. The tumor was excised. The maximum diameter of the mass was 8-cm. The cut surface had gray-white appearance with haemorrhagic infiltrations and fibroelastic constitution. Histologically, the lesion was composed of stellate and spindle-shaped neoplastic cells embedded in a myxoid and collagenous stroma. Nuclear atypia and mitoses were absent. The lesion had an important vascular component; the blood vessels were of various sizes and had thick or thin walls. The lesion had infiltrative borders. Immunohistochemically, the tumor-cells stained strongly for vimentin and desmin. The tumor-cells were moderately positive for CD34 and oestrogen receptors. The results for cytokeratin AE1/AE3, smooth muscle actin, actin HHF-35, S-100 protein, factor 8, factor XIIIa and progesterone receptors were negative. The histological and immunohistochemical findings were compatible with the diagnosis of an aggressive angiomyxoma of the vulva. **Conclusion:** Aggressive angiomyxoma of the vulva should be distinguished from the benign and malignant myxoid tumors or tumor-like conditions of vulva. The pathologic and immunohistochemical characteristics, the difficulties in determining the surgical margins and the treatment of this tumor are discussed. Also, the international literature is reviewed.

**20. Isolated torsion of the fallopian tube: A case report and review of the literature**

Antoniou N., **Varras M.**, Bartzokas A., Kitsiou E., S. Stefanaki S., Akrivis Ch.  
5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p106.

**21. Autoimmune oophoritis: Report of two cases and review of the literature**

Stefanaki S., Akrivis Ch., **Varras M.**, Kyparos J., Demou A., Antoniou N.  
**5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p104.**

**Abstract:**

**Introduction:** Autoimmune oophoritis is a rare condition, which provokes primary ovarian failure with either primary amenorrhea or secondary amenorrhea preceded by progressive oligomenorrhea and hypomenorrhea. The purpose of this study is to document the histological findings in ovarian tissues from two patients with autoimmune oophoritis. **Cases:** Two cases of autoimmune oophoritis are presented, whose pathologic findings were consistent with the international literature. Both

cases were histologically characterized by lymphocytic and plasma cell infiltration in relation to developing follicles, but not to primordial follicles. Also, the clinical findings of these cases are reported. **Conclusion:** Patients with autoimmune oophoritis should be recognized by ovarian biopsy and pathologic diagnosis because these patients are at increased risk of developing other autoimmune disorders.

**22. Primary postpartum haemorrhage due to a large submucosal nonpedunculated uterine leiomyoma: a case report and review of the literature.**

Akrivis Ch., **Varras M.**, Bellou A., Kitsiou E., Stefanaki S., Antoniou N.

**5th Congress of European Society of Gynecology, Rhodes, Greece, October 9-11, 2003; Abstract Book, p98.**

**23. Conserving fertility during ovarian tumor surgery for germ cell tumor (dysgerminoma) in adolescence: case report.**

Michalodimitrakis N., Antoniou N., **Varras M.**, Mpasiotou V., Mainta Evg., Michalodimitraki L, Paissios P.

**14th WORLD CONGRESS ON PEDIATRIC & ADOLESCENT GYNECOLOGY, GREECE, MAY 8-11/2004 ATHENS; Abstract Book, 14th WORLD CONGRESS ON PEDIATRIC & ADOLESCENT GYNECOLOGY, GREECE, MAY 8-11/2004 ATHENS, p.95 (P36).**

**24. Prenatal evaluation of Thoraco Omphalopagus conjoined twins by means of ultrasonography and MRI.**

Salabasis K., Kallinteri Ch., Mitsakos K., Metsis G., **Varras M.**, Panagiotopoulos N., Kassanos D., Kelekis N., Salamalekis E.

**XIX European Congress of Perinatal Medicine, Athens, Greece, 13-16 October 2004; Abstract Book.**

**25. Antenatal sonographic diagnosis of pharyngeal teratoma.**

**M. Varras**, Ch. Akrivis, S. Karadaglis, Ch. Plis, G. Tsoukalos, I. Ladopoulos

**Poster Presentation: The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.**

**Abstract:**

**INTRODUCTION:** Teratomas are the most common tumors. They are usually localized in the sacrococcygeal area, while the pharyngeal localization is very rare. The number of cases of stomato-pharyngeal teratomas detected prenatally via sonography is very small. **CASE:** We present the case of a 24-year-old primipara at 18 weeks' gestation, that at the routine ultrasound scan, the fetus was found with a echogenic mass, filling the stomato-pharyngeal cavity and protruding from the mouth. Other abnormalities were not found. Termination of pregnancy was achieved using misoprostol. A female stillborn fetus with a weight of 250 g and length of 25.5 cm was delivered. The postmortem and pathologic examination confirmed the diagnosis. **CONCLUSION:** Pharyngeal teratomas can be diagnosed with the use of ultrasounds in utero in order to terminate the pregnancy in early time.

**26. Uterine prolapse during pregnancy**

**M. Varras**, Ch. Akrivis, S. Karadaglis, Ch. Plis, G. Tsoukalos, I. Ladopoulos

**Poster Presentation: The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.**

**Abstract:**

**INTRODUCTION:** Uterine prolapse is very rare during pregnancy. It can be associated with maternal discomfort, cervical desiccation and ulceration, urinal tract infection, acute urinal retention, spontaneous abortion and preterm labour. We present a case of uterine prolapse, which was managed successfully during pregnancy and labor.

**CASE:** A 31-year-old woman, gravida 3, para 2, presented in the antenatal outpatient clinic at 32 weeks of gestation complaining of something coming out from her vagina. The patient had no medical history. She experienced the same symptoms during her previous pregnancy that disappeared postpartum. Physical examination revealed an elongated cervix, with moderate edema, but without ulcerations. The cervical os was closed. The patient was managed conservatively with bed rest and evaluation every 2 weeks. During the course of pregnancy, the cervix has been further elongated. At 39 weeks of gestation, she was admitted to the hospital with spontaneous onset of labor and a cervical dilatation of 5 cm. She gave birth to a male of 3650 g. Her postpartum course was satisfactory and she discharged from hospital on day 3. The follow up after 3 months revealed complete resolution of uterine prolapse. **CONCLUSION:** The diagnosis of uterine prolapse during pregnancy and frequent follow-ups are necessary in order to prevent maternal and fetal complications. The successful management of the pregnancy should be individualized but bed rest should be suggested at all pregnancies.

**27. Prenatal diagnosis of congenital cystic adenomatoid malformation of the fetal lung**

**M. Varras**, Ch. Akrivis, S. Karadaglis, Ch. Plis, G. Tsoukalos, I. Ladopoulos

**Poster Presentation: The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.**

**Abstract:**

**INTRODUCTION:** Congenital cystic adenomatoid malformation of the fetal lung is an extremely rare developmental abnormality characterized by an excessive overgrowth of the terminal respiratory bronchioles at the expense of the saccular spaces. Sonography is important for the prenatal diagnosis. We report the diagnosis of a congenital cystic malformation of the lung in utero and present the ultrasonographic findings and the postmortem pathology of this entity. **CASE:** A 33-year-old primipara was presented for a routine ultrasonographic examination at 20 weeks' gestation; congenital adenomatoid malformation of the fetal lungs, type II, was diagnosed. On the right side of the chest an area with a maximum diameter of 18.5 mm and with small cystic lesions was recognized. The maximum diameter of the cysts was found to be 0.5 cm. There were no fetal ascites, mediastinum shift, pericardial effusion, pleural effusion, congenital diaphragmatic hernia or other fetal abnormalities. The couple decided to terminate the pregnancy, which was carried out using misoprostol. A female fetus was delivered, weighing 330 g. The postmortem examination showed a congenital cystic adenomatoid malformation of the right middle lobe of the lung, which was histologically classified as type II. No

other congenital abnormalities were found. Pathologically, the cysts had the appearance of bronchiolus-like structures and were lined with cuboidal and focally columnar epithelium; distended alveoli were present. The airways were normal in structure. The fetal karyotype was 46, XX. **CONCLUSION:** We describe the ultrasound and pathologic findings of a rare case of congenital cystic adenomatoid malformation of fetal lung-type II and discuss its aetiology.

## **28. Prenatal diagnosis of fetal hemivertebra**

**M. Varras**, Ch. Akrivis, S. Karadaglis, Ch. Plis, I. Ladopoulos, N. Antoniou

**Poster Presentation:** The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.

### **Abstract:**

**INTRODUCTION:** Hemivertebra is a rare congenital malformation of the spine, where only one side of the vertebral body develops, leading to deformation of the spine, such as scoliosis, lordosis, or kyphosis. **CASE:** We present the ultrasonographic findings of a fetus with solitary hemivertebra diagnosed at 20 weeks' gestation. The triple test at 16 weeks of gestation was negative: AFP 42 ng/ml (MoM=0.992) , E3 3.8 nmol/l (MoM=1.834) ,free  $\beta$ -hCG 28 ng/ml (MoM=2.806) . The ultrasound scan at 16 weeks' gestation showed no malformations. At the b-level ultrasound scan at 20 weeks' gestation the biparietal diameter was 46mm, the abdominal circumference 145 mm, the fetal femur length 32mm and the possible fetal weight 348 g. Amniotic fluid was at normal limits. However, a distortion at the lubar legion of the spine, at the longitudinal plane was demonstrated. A small triangular bony structure was wedged against the normal vertebral bodies. No other abnormalities were detected. The initial diagnosis was single hemivertebra and the parents decided to terminate the gestation. The labour was induced using misoprostol and the ultrasonographic findings were confirmed with a simple x-ray of the stillbirth fetus and with pathologic examination. **CONCLUSION:** The characteristic US findings of hemivertebra help at the early detection of this situation in order the parents to have on time information to make a decision to proceed or not with their gestation.

## **29. Spontaneous posterior uterine wall rupture at 37 weeks' gestation with history of suction curettage: our experience of a rare case with review of the literature.**

Ch. Akrivis, **M. Varras**, G. Tsoukalos, S. Karadaglis, I. Ladopoulos, N. Antoniou

**Poster Presentation:** The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.

### **Abstract:**

**Background:** Uterine perforation or uterine wall defect is an uncommon but serious complication of elective abortion or evacuation of placental parts retained in the uterine cavity during the puerperium. The most hazardous problem of uterine perforation is uterine rupture during a subsequent pregnancy, with can be fatal for both fetus and mother. **Case:** A 44-year-old woman, gravida 5, para 2 with a history of two elective suction abortions went to the local Hospital of a small Greek Island at 37 weeks with spontaneous rupture of membranes half an hour before admission. Prenatal care was uncomplicated, ultrasonographic evaluation at 22 weeks revealed

a singleton fetus, posterior placenta and normal amniotic fluid volume. The patient denied vaginal bleeding, drug use and hypertension during pregnancy. On admission the patient was calm; temperature was 36.70 C, blood pressure 120/65 mmHg and pulse 78 beats/min. On examination, the fetus presented as cephalic and the cervix was closed with 30% effacement. Complete blood cell count, clotting factors and urinalysis results were normal. The fetal heart rate tracing was reactive with a baseline of 140 beats/min, and no uterine contractions were noted on the external tocodynamometer. Labor was induced using oxytocin, with contraction monitoring by external monitor. One and half hours later the woman complained for sudden abdominal pain and profound fetal bradycardia occurred. The obstetrician stopped oxytocin, placed the patient in left lateral decubitus position and gave oxygen and intravenous fluid for intrauterine resuscitation. Soon after that loss of beat-to-beat fetal heart was noted. The Obstetrician examined her and found no vaginal bleeding and a closed cervix. Her abdomen showed lower tenderness. He decided to transfer the patient in a tertiary center. Therefore, the patient was arrived by ambulance at "Chatzikosta" General Hospital four and half hours later and was taken immediately to the operation room. Small amount of blood was emanating from the cervical os. During the emergency laparotomy there was free blood in the abdomen, and the fetus and the placenta were completely exteriorized from the uterus. A stillborn male infant weighing 3.400 g was removed from the abdomen. Also, the placenta was removed manually from the abdomen and the free blood was irrigated. The uterus was exteriorized for examination and a 7-cm longitudinal defect in the posterior surface of the uterus from the fundus to the supracervical area was identified as the source of rupture. The myometrium surrounding the rupture appeared normal, and the uterus was well contracted. The uterine vessels were not torn but small actively bleeding vessels in the tear were present. The margins of the uterine rent were freshened and closed with a double layer No 1 Vicryl continuous locked suture. However, a cesarean hysterectomy was performed because hemostasis was not achieved although the intravenous administration of oxytocin and ergotamine. The patient's pre- and postoperative hemoglobin levels were 11.5 g/dl and 9 g/dl respectively. She received two units of fresh frozen plasma intraoperatively. Her postoperative period was uneventful and was discharged from hospital 7 days later. **Conclusion:** Spontaneous uterine rupture is a rare but serious and catastrophic event. Sudden abdominal pain and fetal distress after previous trauma to the uterus from prior suction abortion should always prompt consideration of uterine rupture as a possible cause.

### **30. Disruption of prior uterine incision following misoprostol for second trimester abortion in a woman with previous cesarean section**

**M. Varras**, Ch. Akrivis, S. Karadaglis, Ch. Plis, G. Tsoukalos, I. Ladopoulos

**Poster Presentation:** The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.

#### **Abstract:**

**Background:** Few cases with uterine rupture during the second trimester with a previous uterine scar have been reported in the literature. **Case:** A 23-year-old woman with a prior low transverse cesarean section presented at 22 weeks' gestation

for pregnancy termination because of multiple fetal abnormalities. She was given 800 microg misoprostol intravaginally every 4 h until regular contractions began. After the third dose she had vaginal bleeding and severe uterine contractions. She aborted completely 2 h later the last dose. Under general anesthesia, uterine rupture was diagnosed at site of the previous cesarean section by manual vaginal examination. A laparotomy revealed a 7-cm anterior uterine wall rupture at the site of the previous cesarean section with considerable hemorrhage into the abdominal cavity. The uterus was repaired. **Conclusion:** Misoprostol use in the second trimester in a woman with previous cesarean section can lead to uterine rupture.

### **31. Emergency obstetric hysterectomy in two tertiary centers: a clinical analysis of 11 years experience.**

**M. Varras**, Ch. Akkrivis, S. Karadaglis, N. Kanellopoulos, N. Antoniou, I. Ladopoulos

**Poster Presentation: The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.**

#### **Abstract:**

**PURPOSE:** Emergency obstetric hysterectomy is a life saving procedure, which is usually performed as a last resort for a variety of indications with massive uncontrollable intra-operative or postpartum hemorrhage. The purpose of this study was to present the frequency, the indications and the possible complications related to the emergency postpartum hysterectomy. **METHOD:** In this retrospective clinical study, performed between 1997-2007 at the maternal units of 'TZANEIO' General Hospital of Piraeus and 'HATZIKOSTA' Hospital of Ioannina Greece, we studied all the cases of emergency peripartum hysterectomies to control major postpartum hemorrhage after delivery, following a pregnancy of at least 24 week's gestation regardless of the mode of delivery. The data regarding the frequency of hysterectomies at the totality of the deliveries, the distribution of hysterectomies between normal and operative labors, the indications of hysterectomies, as well as the maternal mortality and fetal early/late morbidity and mortality, were noted and evaluated. **RESULTS:** During the study period there were 16,521 deliveries and 5,360 were by cesarean section. In this period, 12 emergency hysterectomies were performed, with a frequency of 0.0726%; 7 emergency hysterectomies were performed after cesarean section and 5 after normal labor (including vaginal assisted delivery with the use of vacuum). Between the 7 cases after cesarean section, the 4 were after previous cesarean section; 4 of the women were primiparas and 8 multiparas. Abnormal vaginal bleeding was the reason in all of the cases. Indications included uterine atony (4 cases), uterine rupture (3 cases), uterine retroversion (2 cases), abnormal placentation (2 cases) and amniotic fluid embolisation (1 case). The result was 2 maternal deaths and 3 stillborns. No bladder lesions occurred. **CONCLUSION:** Peripartum emergency hysterectomy is an urgent procedure with high risk of blood loss during the operation. The gynecologists should be well trained to perform the operation and taking the on-time the decision for this surgical operation can prevent serious complications. At this study, it is demonstrated that the most common reason is uterine atony (33.3%). Other indications include uterine retroversion, uterine rupture, placenta accreta and amniotic fluid embolisation.

### **32. Large broad ligament myoma in pregnancy**

Ch. Akrivis, **M. Varras**, S. Karadaglis, Ch. Plis, I. Ladopoulos, N. Antoniou

**Poster Presentation: The 7th World Congress in Fetal Medicine, Italy, 22-26 June 2008.**

#### **Abstract:**

**INTRODUCTION:** Benign tumors of smooth muscles (leiomyomas) are the most common tumors of the female genital track. They are easily diagnosed during pregnancy and usually managed conservatively. Non-specific localizations during pregnancy usually cause diagnostic and surgical difficulties. **CASE:** A 34-year-old woman para 3 during routine NT scan at 13 weeks' gestation was found randomly to have a tumor with maximum diameter of 24-cm, that initially was considered to have origin of the right adnexa. The MRI scan showed a large tumor with leiomatous elements that moved the uterus leftwards without the characters of an exophytic with pedicle myoma. No enlarged iliac or aortic nodules were found. It was thought to be a peritoneal mesenchymatic tumor like leiomyoma, leiomyosarcoma or fibrosarcoma. During the laparotomy at 14 weeks' gestation, with Pfannestiel incision, a large tumor inside the broad ligament without connection with the uterus was found. The tumor was completely resected with the larger part of the broad ligament as well. The tumor was a leiomyoma with cystic degenerations. The gestation was continued until term without further complications. **CONCLUSION:** Familiarity of gynecologists and pathologist with the benign tumors of smooth muscular fibres with unusual localization is essential in avoiding over-treatment.

#### **(viii) PRESENTATIONS IN GREEK CONFERENCES**

##### **1. Activation of K-ras oncogene in tumors of the endometrium [in Greek].**

**Varras M.N.**, Koffa M., Koumantakis E., Protopappa E., Ergazaki M., Spandidos DA.

**Presentation:** 6<sup>th</sup> National Congress of Obstetrics and Gynecology, 23-26 of November 1994, Athens.

**Publication:** Book of Abstracts page 102.

**Award in memory of "Ioannis Mantalenakis" from the Greek Society of Obstetrics and Gynecology**

#### **Abstract:**

Endometrial cancer is quite frequent in Greece and seems to be caused by a number of somatic mutations. A genetic transformation is the activation of gene K-ras, by point mutation at codon 12. Recent studies have reported the presence of these point mutations at a rate of 10-37% in endometrial cancers. In this study forty-four (44) cases of endometrial adenocarcinomas preserved in paraffin blocks were examined for the presence of a point mutation in codon 12 of K-ras gene. The samples were classified according to the age of the patients, the degree of histological differentiation, the histological subtypes, and the depth of myometrial filtration. The technique of polymerase chain reaction (PCR) was used to amplify a region of 157 bases of K-ras gene, which contains the codon 12 and the mutations were detected with polymorphism restriction fragment length (RFLP) analysis. Five of the forty-four samples (11.4%) were found to have a mutation at codon 12 of the

gene *K-ras*. Mutations were found in two of the eight patients with adenoacanthoma, in one of the three cases with papillary carcinoma and endometrial adenoacanthoma and in two of the fifteen cases with papillary endometrial carcinoma. Not statistical correlation was found between the presence of mutations and the degree of differentiation or the stage of the tumor, suggesting that activation of the *K-ras* gene occurs possibly at primary stages of endometrial carcinogenesis.

**2. [Involvement of ras oncogenes in the pathogenesis of endometrial cancer]** [in Greek].

**Varras M.N.**, Koffa M., Koumantakis E., Ergazaki M., Protopapa E., Sfiniadakis I., Spandidos D.A.

**Ανακοίνωση:** 1st Congress of the Greek Society of Cervical Pathology and Colposcopy, 1-3 June 1995, Athens.

**Δημοσίευση:** [Colposcopy and Gynaecological Cancer 1995, 1, σελ.:77.](#)

**3. [Examination of response to adjuvant chemotherapy in patients with ras genes mutations in primary epithelial ovarian cancers]** [in Greek].

**Varras M.N.**, Sourvinos G., Flouris G., Lekka-Katsouli I. Koumantakis E., Akrivos Th., Michalas S., Spandidos D.A.

**Presentation:** 7th National Congress of Gynecology and Obstetrics, 14-17 May 1997, Heraklion, Crete.

**Publication:** Book of Abstracts, abstract number 16.

**4. [Detection of human papillomavirus human (HPV) and the K-ras mutations by the technique of PCR in cytological material of cervical carcinomas]** [in Greek]

Papaefthemiou M., **Varras M.N.**, Dopianakis D., Tsiveleka A., Michalas S., Symiakaki E., Spandidos DA.

**Presentation:** 4th National Congress of Cytology, 26-28 March 1998, Athens.

**Publication:** Book of Abstracts, abstract number 30.

**5. The scalpel which is activated by ultrasound: Application "harmonic scalpel"** [in Greek].

Katsetos C., **Varras M.**, Papantoniou N., Weltch C.

**Presentation:** 1<sup>o</sup> Greek National Congress of Gynecologic Endoscopy, 8-10 October 1999, Athens.

**Publication:** Book of Abstracts, page 75.

**Abstract:**

Since the inception of laparoscopic surgery at the late 80s there was an ongoing controversy about the safety of hemostasis between electrosurgery and laser. In recent years the energy through the ultrasounds ("Harmonic Scalpel") for tissue section and hemostasis, has been used in many centers for endoscopic surgery. The "Harmonic Scalpel" consists of a generator, connected with cable, one handle, a blade system and a pedal. The generator is controlled by a microprocessor which generates high frequency energy of 55,000 Hz, which guides the auditory system in the handle. The knife has three positions the blunt, the flat and the acute. The

transducer located at the handle consists of piezoelectric ceramics which convert the electricity from generator into mechanical vibrations at the attached scalpel through an extension rod. The more elongated pulse slippage of the scalpel is of the order of 50 to 100 microns, depending on the type of blade and the power level (5 levels). The extension rod is supported by a system of silicone rings to absorb the laterally extending vibration and to convert it longitudinally without vibration and noise. The "Harmonic Scalpel" provides to the surgeon and the gynecologist in particular, many advantages compared with electrosurgery and lasers. **1)** Hemostasis can be better controlled by adjusting simultaneously the duration of activation and the power level in contrast to the unipolar or bipolar diathermy which are less controlled energy sources. Comparing roughly the same power levels and time of application of electrosurgery and harmonic scalpel, much less damage to the depth and volume of the adjacent tissues are found in the case of harmonic scalpel use. **2)** Using the technology of ultrasound less smoke is generated. With the technology of ultrasonics the tissues are cut and the hemostasis is performed at lower temperatures <100°C. With the electrosurgery the hemostasis is achieved through overheating and sloughing of tissues. The tissue cutting with the first method is accomplished by raising the tissue temperature and rapid evaporation—"explosion" of the intracellular water, while the carbonization creates enough tobacco which affects visibility. **3)** With ultrasound not electricity is channeled through the patient, thus eliminating the risk of electric shock. **4)** More time for hemostasis achievement is needed using harmonic scalpel compared to electrosurgery and laser but it has the advantage of not need for changes of the laparoscopic instruments. Applications to Gynecology: **i)** Adhesiolysis, **ii)** Laparoscopic assisted vaginal hysterectomy, **iii)** Ovarian cystectomy, **iv)** Salpingo-oophorectomy, **v)** Myomectomy, **vi)** transcervical endometrial ablation, **vii)** Selective pelvic lymphadenectomy. The laparoscopic technology triggered by ultrasounds is easier to be used and its implementation costs are compared with the other methods providing the gynecologist with larger safety limits. After five years of commercial application, it has an important place in our surgical options because the advantages are obvious.

#### **6. [Intraperitoneal bupivacaine for post-operative pain reduction for gynecological laparoscopic surgery] [in Greek].**

**Varras M.**, Miskry T., Katsetos Ch., Ruston J., Magos A.

**Presentation:** 1<sup>o</sup> Greek National Congress of Gynecologic Endoscopy, 8-10 October 1999, Athens.

**Publication:** Book of Abstracts, page 79.

<http://www.hopkinsmedicine.org/fertility/services/>

#### **Abstract:**

**Purpose:** Laparoscopic surgery could mean minimal pain. Several methods have been described to reduce this pain. The purpose of this study is to determine the value of intraperitoneal infusion of the long lasting local anesthetic (bupivacaine) to reduced need for pain medication postoperatively in gynecological laparoscopy.

**Method:** A total of 34 patients were examined. Seventeen patients who underwent surgical laparoscopic operations were taken 10 ml 0.5% bupivacaine in 500 ml saline at the end of surgery intraperitoneally. Patients who underwent combined surgery

(eg laparoscopically assisted vaginal hysterectomy) or were suffering from heart disease or had a known hypersensitivity to the drug were excluded from the study. Total administration of analgesics during surgery and postoperatively recorded and converted to equivalent doses of subcutaneous morphine. These results were compared with the analgesic needs of the patients' archives of 17 women not were not receiving intraperitoneal bupivacaine infusion. Additionally, the group of bupivacaine completed one 10-centimeter optical analogue pain scale to assess pain of intra 4 and 24 hours postoperatively. **In conclusions:** Intraperitoneal infusion of bupivacaine at the end of gynecologic laparoscopic surgery appears to reduce significantly the need for postoperative analgesics. The rates of postoperative pain suggest that this effect is long lasting.

**7. [The educational role of multimedia in gynecological laparoscopic surgery] [in Greek].**

**Varras M.,** Linehan J., Magos A.

Ανακοίνωση: 1<sup>ο</sup> Πανελλήνιο Συνέδριο Γυναικολογικής Ενδοσκόπησης, 8-10 Οκτωβρίου 1999, Αθήνα.

Δημοσίευση: Βιβλίο Περιλήψεων, σελ. 88.

**8. [Laparoscopic conservative removal of ovarian dermoid cyst in the bag] [in Greek].**

**Varras M.,** Davies A., Miskry T., Magos A.

**Presentation:** 1<sup>st</sup> National Congress of Gynecologic Endoscopy, 8-10 October 1999, Athens.

**Publication:** Abstract Book, page 64.

**Abstract:**

**Purpose:** Dermoid cyst is the most common type of tumors observed during the reproductive life of woman, and generally conservative therapy is indicated for the maintenance of the ovary. The advantages of laparoscopic surgery for the patients include reducing time of hospitalization and convalescence. However theoretically intraperitoneal rupture of the dermoid cyst and output of its content may cause humoral peritonitis and moreover there is a 2% to 3% risk of malignant transformation of a seemingly benign dermoid cyst. Herein, we introduce laparoscopic excision of dermoid cysts within the bag in order to reduce the risk of peritoneal contamination. **Method:** After careful examination of the peritoneal cavity and suction of peritoneal leachate, an intraperitoneal bag was introduced. We use the sterile wrapping of the disposable plastic suction tubes as it has no costs, it is transparent and every time can be adjusted in size proportional to the size of the ovarian cyst. We open the bag at the posterior space of Douglas using atraumatic laparoscopic forceps and the corresponding adnexa is placed inside the bag. Then, the opening of the bag is closed by one of the three clamps in order to avoid the exit of the ovary from the bag during operation. Then, laparoscopic ovarian cystectomy is done using tongs arrest and laparoscopic scissors. In case of rupture of the dermoid cyst, its content remains within the plastic bag. Thus its contents can be aspirated and the cyst can be washed before continuing the operation. When the resection of the bladder is completed, normal ovarian tissue and the fallopian tube are placed

back in the pelvis outside the plastic sac. The opening of the bag is closed with suture and the cyst is removed through a posterior colpotomy. The ovary is sutured if required. **Results:** We encountered four patients with this technique with dermoid cyst diameters from 4 to 7 centimeters. One of the four has broken into the bag peritoneal contamination was observed. In all of the four cases, the pathologic examination showed mature teratomas. **In conclusion:** Laparoscopic conservative remove of the dermoid cysts within a bag minimize the risk of intraperitoneal infection with its contents and increases the safety of endoscopic treatment of this neoplasia.

**9. [Sclerosing stromal tumor of the ovary: Report of a case and review of the literature] [in Greek].**

**Varras M.,** Stylianidou A., Akrivis Ch., Galanis P., Fylaktidou A., Antoniou N.

**Presentation:** 8<sup>th</sup> Greek National Congress of Obstetrics and Gynecology, 25-28 May 2000, Thessaloniki.

**Publication:** Abstract Book, page 185, number 179.

**Abstract:**

**Purpose:** The sclerosing stromal tumor (SST) of the ovary is an extremely rare benign neoplasm. Since first described in 1973 by Chalvardjian and Scully today have announced fewer than 100 cases. It occurs predominantly in the second and third decades of life and usually manifests clinically with infertility, but without causing hormonal disturbances, in most cases. Histologically, it is characterized by cellular heterogeneity, prominent vascularity and pseudolobular pattern due to alterations of areas with several cells and areas with sclerosis and edema. Immunohistochemically, interesting as regards the histogenesis is the focal positivity for actin smooth muscle (SMA) and desmin. The differential diagnosis of the tumor should include other stromal tumors of the ovary such as thecomas, fibromas, and lipoid-cellular (steroid) tumors of the ovary. **Material and Methods:** We present a new case of sclerosing stromal tumor (SST) of the ovary in a 21 year old woman, who was admitted for infertility. This study analyzes the morphological, histochemical and immunohistochemical characteristics of the tumor as well as the expression of hormonal receptors. **Results:** It is demonstrated that the neoplasm is hormone-dependent, with focal positivity for actin in smooth muscle fibers. **Conclusions:** Further discussion is given about the characteristics of the tumor with review of the literature and highlight in those findings that help in the differential diagnosis.

**10. [Results of the action of intravaginal tablet Vagifem for the treatment of atrophic vaginitis] [in Greek].**

Akrivis Ch., Thodos A., **Varras M.,** Galanis P., Fylaktidou A., Antoniou N.

**Presentation:** 8<sup>th</sup> Greek National Congress of Obstetrics and Gynecology, 25-28 May 2000, Thessaloniki.

**Publication:** Abstract Book, page 372, number 366.

**Abstract:**

**Purpose:** Atrophic vaginitis is a chronic problem of postmenopausal women and can be treated with topical therapy or in cases where systemic treatment is

contraindicated or for personal desire of the woman. The purpose of this study was to investigate the efficacy of the intravaginal tablet Vagifem (25 µg 17-beta estradiol) for the treatment of atrophic vaginitis in postmenopausal women and to examine the systemic absorption of 17-beta estradiol. **Material and Methods:** Ninety-one postmenopausal women with atrophic vaginitis were treated for three months with vaginal tablets Vagifem. During the first two weeks of the vaginal tablets were administered daily and then twice per week. The study included repetitive assessments of the symptoms of atrophic vaginitis, check for mastodynia and measurements of the levels of serum 17-beta estradiol, FSH and LH. Control group was not used. **Results:** The results showed that the intravaginal tablet Vagifem essentially nullify the incidence of vaginal dryness, itching and dyspareunia from the first month of treatment. The plasma concentration of 17-beta estradiol during treatment differentiated statistically significantly ( $p < 0.001$ ), but remained within the post-menopausal levels. Mastodynia which occurred at a rate of 5.8% was significantly reduced to 2.5% during treatment. **Conclusions:** The results suggest that the use of intravaginal tablets Vagifem is effective and safe method of treatment of atrophic vaginitis in postmenopausal women.

#### **11. Pyoperitonitis as a complication of assisted reproduction.**

**Varras M.,** Antoniou S., Varela V., Georgiadou D., Apessou D., Antypa E., Paisios P.

**Presentation:** 10<sup>th</sup> PanCretan Medical Conference, 9-12 November 2000, Rethymno, Crete, Greece

**Publication:** Book of Abstracts, page 340.

#### **12. [Impaired kidney function of ovarian cancer] [in Greek].**

**Varras M.,** Antoniou S., Eleftheriou M., Georgianou D., Varela V., Paisios P.

**Presentation:** 10<sup>th</sup> PanCretan Medical Conference, 9-12 November 2000, Rethymno, Crete, Greece

**Publication:** Book of Abstracts, page 339.

#### **Abstract:**

**Purpose:** Ovarian cancer rarely causes obstruction of the urinary tract. Its most common cause of gynecological cancers is the cancer of the cervix, which causes obstruction of urine flow of into the pelvic portion of ureters (Geisler et al, 1994). The purpose of this paper is to present a rare case of hydronephrosis and impaired function of the right kidney caused by a tumor of the right ovary. **Material and Methods:** Patients 55 years showed constipation of eight months and then the last two months, urinary incontinence and urinary frequency. The last fortnight showed abdominal distension and bloating. In intravenous urography a large degree of delay was observed in apocrine and drainage function of the right kidney with pyelocalyceal stop. The CT scan with the aid of contrast revealed bilateral hydronephrosis, mainly at the right kidney as well as at the position of the right uterine adnexa the existence of an oval tumor measuring 5x10x6-cm with the presence of diaphragms within. The radioactive nephrogram revealed reduction of the invasive phase and overtime of the extension phase of the right kidney. The right kidney accounted for 37% and the left for 73% of the total renal function. **Results:** During the exploratory laparotomy a large tumor of the right ovary was found and

the frozen biopsy showed the presence of a mucinous ovarian cystadenocarcinoma. The tumor was invasive to bladder, and the cervix was firmly attached to parametria. After surgical staging and closure of the abdominal wall was found anuria not responding to intravenous furosemide. Placement of pig tail with cystoscopy failed and therefore percutaneous left kidney nephrostomy was performed. The postoperative course of the patient was good. Both bladder Foley catheter and urine nephrostomy yielded urine. The patient receives adjuvant therapy based on platinum. **Conclusion:** Obstruction of ureters and kysteroouritiriks contribution can be caused by ovarian cancer. **Reference:** Geisler J.P., Perry R.W., Ayres G.M., Holland T.F. 3<sup>rd</sup>, Melton M.E., Geisler H.E. Ovarian cancer causing upper and lower urinary tract obstruction. Eur. J. Gynaecol. Oncology 1994, 15, 343-344.

**13. [Tumoral ovarian lesions in women over 30 years old] [in Greek].**

**Varras M.,** Kotzapanagiotou K., Stylianidou A., Akrivis Ch., Stefanaki S., Antoniou N.

**Presentation:** 10<sup>th</sup> PanCretan Medical Conference, 9-12 November 2000, Rethymno, Crete, Greece

**Publication:** Book of Abstracts, page 341.

**Abstract:**

**Purpose:** Ovarian cancer is the leading cause of death among women with gynecologic cancers and occurs at 23% of all gynecological tumors. Ovarian tumors can occur in women of any age. However, there are differences in histological type of ovarian tumors depending on the age of women<sup>1</sup>. The purpose of this study is the histological analysis of ovarian tumors in women over the 30 years. **Material and methods:** We analyzed randomly 150 cases of women who were operated at the Obstetrics & Gynaecology Department of "G. Hatzikosta" General State Hospital, Ioannina because of an ovarian tumor. The analysis included patient's age, histological type, histological grade and FIGO stage of cancers. The tumors were classified histologically by WHO<sup>2</sup>. The microscopic examination of the tissue specimens was performed at the Pathology Department of the same hospital. **Results:** Of the 150 cases with ovarian tumors studied were found functional ovarian cysts at 49 cases (32.6%), simple endometrioid cysts at 13 cases (8.7%), tubo-ovarian abscesses at 4 cases (2.7%), benign tumors at 60 cases (40%), tumors with potential malignancy at 9 cases (6%) and malignant tumors at 15 cases (10%). The benign ovarian tumors included 31 epithelial tumors (52%), 19 neoplasms of germ cells (32%) and 10 neoplasms of germ cells sex cord stromal tumors (16%). Benign epithelial tumors included 14 mucinous cystadenomas, 15 serous tumors and 2 cystadenomas Brenner. Neoplasms of germ cells sex cord stromal tumors included 3 fibromas, 6 thecomas and 1 unclassified. Benign tumors of germ cells included 19 cases of mature teratoma (dermoid cysts). Potential malignant tumors included 5 cases of borderline malignancy and 4 granulosa cell tumors. The malignant tumors were 12 primary ovarian adenocarcinoma and 3 metastatic. At a rate of 6.7% endometrioid adenocarcinoma development at the ovarian endometrioid cyst wall was observed. The mean age of women with borderline ovarian malignancy was 47 years, with granulosa cells tumors 56 years and with primary adenocarcinoma 57 years. The incidence of primary adenocarcinomas has increased in line with the mean age of patients from 25% in women between 30 and 49 years to 75% in

women 50 years and older. The highest frequency of borderline malignant tumors (80%) was observed in women under the 50 years of age. **Conclusions:** The overall risk in women over 30 years who were operated on for ovarian tumors to have a malignant ovarian tumor is 10%, while to potential borderline malignant tumor is 6%. The incidence of primary ovarian adenocarcinomas is three times higher in women over 50 years compared with younger patients. Also, the possibility the wall of an endometrioid cyst to have endometrioid adenocarcinoma is found to be 6.7%. References: (1). Merina M.J., Jaffe G. Age contrast in ovarian pathology. *Cancer* 1993, 15, 537-544. (2). Gore H. Histopathology of ovarian cancer. *Semin. Surg. Oncol.* 1994, 10, 255-260.

#### **14. [Findings of uterine curettage in postmenopausal women with vaginal bleeding] [in Greek].**

**Varras M.**, Kotzapanagiotou K., Stylianidou A., Akrivis Ch., Stefanaki S., Antoniou N.

**Presentation:** 10<sup>th</sup> PanCretan Medical Conference, 9-12 November 2000, Rethymno, Crete, Greece

**Publication:** Book of Abstracts, page 342.

#### **Abstract:**

**Purpose:** About 20% of visits of women to the gynecologist is due to abnormal vaginal bleeding<sup>1</sup>. Following the dogma that "any abnormal uterine bleeding after menopause is suspicious for carcinoma until proven the oposite" thousands cervical dilations and curettage are performed each year<sup>2</sup>. The purpose of this study is to determine the findings of fractional curettage of the uterine cavity in postmenopausal women with vaginal bleeding. **Material and Methods:** We randomizely examined the histological reports from 200 postmenopausal women submitted to hospital for cervical dilation and fractional curettage of the uterine cavity because of vaginal bleeding. The operations were performed at the Obstetrics & Gynaecology Department of "G. Hatzikosta" General State Hospital, Ioannina and the microscopic examination was perfomed at the Pathology Department of the same hospital. **Results:** Follicular phase, poorly productive follicular phase or residual secretory phase and inactive or deactivative endometrium were diagnosed at a ratio of 16.5% (33/200), atrophic endometrium at 18% (36/200) and endometritis in 3.5% (7 / 200). Endometrial polyps were found at 20 cases (10%), endometrial hyperplasia at 33 cases (16.5%), while coexistence of enometrial polyp and endometrial hyperplasia at 12 cases (6%). Of the total of 45 endometrial hyperplasias 19 were simple (42%), 12 complex (27%), 9 combination of simple and complex (20%) and 5 atypal (11%). Adenocarcinomas of the endometrium were found at 8.5% (17/200). The histologic types of endometrial adenocarcinomas included 9 endometrioid, 4 papillary serous, 1 adenosquamous, 1 clear cell and 2 mixed types. Inadequate specimen for histological diagnosis was observed in 21% of cases (42/200). **Conclusions:** On the fractional curettage of the uterine cavity in women with postmenopausal vaginal bleeding endometrial cancer is diagnosed at a frequency of only 8.5%. Noteworthy is the fact that with the fractional curretage of endometrial cavity in a significant persentage of 21% the specimen is inadequate for pathologic examination. **References: (1).** Ben-Yehyda O.M., Kim Y.B., Leuchter R.C. Does hysteroscopy improve upon the sensitivity of dilation and curettage in the diagnosis

os endometrial hyperplasia or carcinoma? Gynecol. Oncol. 1998, 68, 4-9. **(2)**. Neis K.J., Brandner P., Hepp H. Hysteroscopy, Text Book and Atlas. Thieme Medical Publishers, Inc. 1994, pp: 79-80.

**15. [Histopathological findings of endocervix and endometrium in women aged 50 years and older who underwent diagnostic fractional curettage] [in Greek].**

Basiotou V., Antoniou S., **Varras M.**, Varela V., Georgiadou D., Paisios P.

**Presentation:** 2<sup>o</sup> Greek National Congress of Climacterium and Menopause, Athens 1-3 December 2000.

**Publication:** Abstract Book, number 4.

**Abstract:**

**Purpose:** The purpose of this study was to investigate the histopathological findings of the endocervix and endometrium in women aged 50 years and older, who underwent diagnostic fractional curettage for either one asymptomatic polyp of the endocervix of the uterus or abnormal vaginal bleeding or because of abnormal sonographic findings of the endometrium. **Material and Methods:** The study included 400 women aged 50 years and older, who underwent diagnostic fractional curettage Gynaecology Department at the Regional General Hospital of Athens "G. Gennimatas". Histologic examination of specimens were performed in the Pathology Department of same hospital. Histopathologic findings of endometrial materials were classified into the following categories: 1) without pathological findings, 2) endometrial polyps only, 3) endometrial hyperplasia, 4) endometrial adenocarcinoma, 5) endometritis, 6) inflammatory lesions endocervix, 7) endocervical polyps alone, 8) cervical cancer, 9) coexistence of endocervical and endometrial polyp, 10) coexistence of endocervical polyp with endometrial hyperplasia, 11) insufficient material for pathological examination. The category without pathological findings included atrophic, productive and secretory endometrium. **Results:** Endometrial histopathology included 134 cases without pathological findings (33.5%), 1 case of endometritis (0.25%), 33 cases of endometrial polyps only (8.25%), 18 cases of endometrial hyperplasia (4.5%) and 31 cases of endometrial adenocarcinomas (7.75%). Regarding endocervical histopathology in 14 women inflammatory lesions were found (3.5%), in 86 women only endocervix polyps (21.5%) were found, whereas in 5 cases cancer was observed (1.25%). Coexistence of endocervical and endometrial polyps was observed in 15 cases (3.75%), ie in a ratio of 15% of all cervical polyps (15/103). Coexistence of endocervical polyp with endometrial hyperplasia was observed only in 2 cases (0.5%). In total of 400 diagnostic fractional curettages insufficient materials for pathological examination was sent at a rate of 15.25% (61/400). The histologic types of endometrial adenocarcinomas included 20 endometrioid, 8 serous papillary, 2 clear cell and 1 adenoacanthoma. **Conclusion:** Endometrial cancer is found in only 7.75% in women aged 50 and older, undergoing fractional curettage because of abnormal vaginal bleeding or asymptomatic endocervical polyp of the uterus. Of all endocervical polyps of the uterus, the frequency of coexistence with endometrial polyps or endometrial hyperplasia are 15% and 1.9% respectively.

**16. [Stromal polyp with endometrial transformation in a postmenopausal patient receiving long-term tamoxifen for breast cancer: Report of a case and review of the literature] [in Greek].**

Antoniou S., Basiotou V., **Varras M.**, Eleftheriou M., Manika Z., Paisios P.

**Presentation:** 2<sup>o</sup> Greek National Congress of Climacterium and Menopause, Athens 1-3 December 2000.

**Publication:** Abstract Book, number 8.

**Abstract:**

**Purpose:** Tamoxifen is a nonsteroidal antiestrogen that is extensively used as adjuvant therapy for primary breast cancer in both premenopausal and postmenopausal women. The benefits of this therapy include increased patient survival and disease-free period. Tamoxifen has a complex mechanism of action and competitive agonistic estrogenic properties depending on the target organ. Its action in the endometrium has been associated with development of polyps, hyperplasias and cancers because of estrogen agonist properties. We present a case of postmenopausal woman who developed a very sizeable endometrial polyp with stromal transformation, while received tamoxifen as adjuvant treatment for breast cancer. **Case report:** Patient 73 years old was admitted to emergency gynecological outpatient clinic because of vaginal bleeding. In her personal history she reported previous treatment with tamoxifen daily for four years due to resected breast cancer four years ago. The patient did not receive another hormonal therapy or chemotherapy. Monitoring the endometrium with curettage or hysteroscopy was not done. During the pelvic examination a sizable prolapsed tissue mass from the uterine cavity with endometrial texture, was observed at the entrance of the vagina. Under general anesthesia, the patient underwent surgery with removal of the large mass with rotation around its axis. After that, curettage of endocervix and endometrium was done. Macroscopically the tumor had size of 9.5X9X5-cm with deep red, smooth and raggedness outer surface. Microscopic examination demonstrated the presence of a case of a twisted adenomatous polyp. In limited areas, giant cells and glands of larger cells with more vesicular nuclei were found. The immunohistochemistry of these cells for keratins was negative. These findings were indicative for stromal transformation of the polyp. **Conclusions:** The endometrial examination of women treated with tamoxifen because of breast cancer is essential. The long-term use of tamoxifen regarding uterine carcinogenesis seems to be related with development of endometrial adenocarcinomas and stromal tumors. The international literature is reviewed for correlation of tamoxifen with the development of adenocarcinomas of the endometrium and stromal uterine tumors.

**17. [Extramedullary hematopoiesis in the isthmus of the uterus] [in Greek].**

**Varras M.**, Stylianidou A., Akrivis Ch., Galanis P., Fylaktidou A. Stefanaki S., Antoniou N.

**Presentation:** 27th Annual Greek Medical Conference, 8-12 May 2001, Athens.

**Publication:** Book of Abstracts, page 73, number 282.

**18. [Heterotopic pregnancy in a natural birth cycle: A pathological situation that should not be forgotten!] [in Greek].**

Akrivis Ch., **Varras M.**, Chatzopoulos G., Karabina E., Antoniou N.

**Presentation:** Annual Conference of the Greek Society of Obstetrics and Gynecology, June 15-16, 2001, Amygdaleonas Kavala.

**Number in the program of the Annual Meeting:** 15.

**19. [Achieving pregnancy after surgical excision of sclerosing stromal ovarian tumor: Report of a case and review of the literature] [in Greek].**

**Varras M.**, Akrivis Ch., Stylianidou A., Chatzopoulos G., Fylaktidou A. Antoniou N.

**Presentation:** Annual Conference of the Greek Society of Obstetrics and Gynecology, June 15-16, 2001, Amygdaleonas Kavala.

**Number in the program of the Annual Meeting:** 14.

**20. [High-grade intraepithelial lesions of the uterine cervix: Cyto-histological correlations] [in Greek].**

Chatzopoulos G., **Varras M.**, Akrivis C., Kotzapanagiotou K., Mermiga E., Antoniou N.

**Presentation:** 2<sup>nd</sup> Greek National Congress of Preventive Medicine, 25-27 January 2002, Athens

**Publication:** Book of Abstracts, page 60, number 29.

**Abstract:**

**Purpose:** The purpose of this study is to determine in the cytological smears the frequency of high grade squamous intraepithelial lesions (HGSIL) in the general population of women and to assess the cyto-histological correlation between HGSIL and histological diagnosis. **Material and Methods:** The study included 8,444 women who attended the outpatient gynecological clinic of "G. Chatzikosta" General Hospital, Ioannina for taking preventive Pap test during the period from 01/01/1995 to 31/12/2000. The cytological classification was according to Bethesda system. Further management of a Pap test with HGSIL included the following: When the lesion of cervical biopsies was evident then biopsies were taken from the suspicious areas. When the lesion of the uterine cervix was no evident macroscopically then colposcopy was performed in order to obtain biopsies from the suspicious areas. In this case and with a satisfactory colposcopy, if the histology of biopsies showed CIN 1 then cervical conization was performed because the Pap test suggested more severe lesions from that of the biopsies. If the histology of the biopsies showed CIN 1 or CIN 2 then cervical conization was performed in order to exclude the possibility of cancer existence at adjacent positions of the biopsies. If the histology of the biopsies showed micro-invasive cancer then conization was performed to specify the existence of micro-invasive or invasive cancer. If the histology of the biopsies showed invasive cancer then radical hysterectomy was done. Also conization was performed on unsatisfactory colposcopy. **Results:** HGSIL at the cervical smears were found in 21 cases. To further control were 18 women (86%). The histological findings included 2 cases with benign lesions (11%), 1 case only with HPV (5.5%), 8 cases with CIN 2 (44%), 2 cases with carcinoma *in situ* (11%) and 5 cases with cancer (28%). In 4 of the 8 cases with CIN 2 lesions coexistence with HPV was found (50%). Micro-invasive cancer of the cervix was found on 2 of the 4 cases with cancer (50%). **Conclusions:** The Pap test in the general population suggested HGSIL at a frequency of 0.25%. The diagnosis of the HGSIL cytology was

overestimated in relation to the histological findings in 17% (3/18), while was underestimated in 28% (5/18).

**21. [Disseminated intravascular coagulation as postoperative complication in a young patient with ovarian adenocarcinoma stage IV].** [in Greek].

Paissios P., **Varras M.**, Polyzos D., Georgiadou D., Samara Ch., Antoniou S.

**Presentation:** 4<sup>o</sup> Greek National Congress of Gynecological Oncology, 28-30 March 2002, Athens.

**Publication:** Archives of Pathology, number of study 57, page 64.

**22. [Torsion of a large paraovarian cyst in a postmenopausal patient: a case report and review of literature]** [in Greek].

Liapis E., **Varras M.**, Antoniou S., Frakala S., Samara Ch., Paissios P.

**Presentation:** 4<sup>o</sup> Greek National Congress of Gynecological Oncology, 28-30 March 2002, Athens.

**Publication:** Archives of Pathology, number of study 65, page 57.

**23. [Simultaneous development of carcinomas in the cervix and uterine endometrium]** [in Greek].

Papaliodi E., Choreftaki Th., Stratigaki Th., Stratigaki A., Tziortzioti V., Apessou D., **Varras M.**, Zaverdinou P., Kyrodemou E.

**Presentation:** Pathology Annual Meeting, April 2002, Volos.

**Publication:** Archives of Pathology, number of study P101.

**24. [Ectopic ovarian pregnancy]** [in Greek].

Despotelli M., Tziortzioti V., Antypa E., Berdousi Ch., Roumelioti A., Kyrodemou E., **Varras M.**, Messini E.

**Presentation:** Pathology Annual Meeting, April 2002, Volos.

**Publication:** Archives of Pathology, number of study P102.

**25. Sonographic findings of tubo-ovarian abscesses]** [in Greek].

Tsikini A., Chatzilira T., Kamariotou E., **Varras M.**, Polyzos D., Apessou D., Tsouroulas M.

**Presentation:** XIII National Congress of Radiology

**Publication:** Book of Abstracts, page 205, number 92.

**Abstract:**

**Purpose:** To describe the sonographic findings of tubo-ovarian abscesses to achieve more correct preoperative diagnosis. **Material and Methods:** Twelve patients who were operated on our hospital during the last 2 years and the existence of tubo-ovarian abscesses were confirmed histologically were included in our study. The ultrasonographic findings were analyzed retrospectively and were correlated with the clinical picture and the number of white blood cells at the time of admission of patients to our hospital. **Results:** The analysis was conducted by transvaginal sonography in 10 patients, while in 2 suprapubic sonography was performed. A tumor was observed in all cases with maximum diameters from 5 to 10 cm The tumor was found in the anatomical location of the ovary in 10 cases and in 2 cases in

the the posterior pouch of Douglas. In 1 case the tumor had cystic appearance, in 2 cases they were with septums and in 8 cases they had cystic with solid components. Vascularization was assessed in 8 patients and was increased in 6. Fluid in the pouch of Douglas was observed in 7 patients. All patients presented with abdominal pain and leukocytosis greater than 11,000. **Conclusion:** The ultrasonographic findings of tubo-ovarian abscesses are not specific. The presence of the tumor in ultrasound in conjunction with the history and clinical picture and the number of white blood cells can lead us to the correct diagnosis.

**26. [Rupture of a tubo-ovarian abscess: Complication after IVF] [in Greek].**

Tsikini A., Antypa E., Chatzilira T., Kamariotou E., **Varras M.**, Polyzos D., Apessou D., Tsouroulas M.

**Presentation:** XIII National Congress of Radiology.

**Publication:** Book of Abstracts, page 205, number 92.

**27. [Antenatal sonographic diagnosis of pharyngeal teratoma.] [in Greek].**

**Varras M.**, Akrivis Ch., Karadaglis S., Plis Ch., Tsoukalos G., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 51, number 25.

**28. [Uterine prolapse during pregnancy] [in Greek].**

**Varras M.**, Akrivis Ch., Plis Ch., Karadaglis S., Tsoukalos G., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 68, number 44.

**29. [Delayed delivery of a healthy twin after intrauterine death and abortion of the first twin] [in Greek].**

Akrivis Ch., **Varras M.**, Plis Ch., Antoniou N., Karadaglis S., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 43, number 18.

**30. [Spontaneous posterior uterine wall rupture at 37 weeks' gestation with history of suction curettage] [in Greek].**

Akrivis Ch., **Varras M.**, Tsoukalos G., Ladopoulos I., Karadaglis S., Antontiou N.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 68, number 45.

**31. [Large broad ligament myoma in pregnancy] [in Greek].**

Akrivis Ch., **Varras M.**, Plis Ch., Karadaglis S., Ladopoulos I., Antontiou N.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 34, number 7.

**32. [Prenatal diagnosis of congenital cystic adenomatoid malformation of the fetal lung]** [in Greek].

**Varras M.**, Akrivis Ch., Plis Ch., Karadaglis S., Antoniou N., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 51, number 26.

**33. [Prenatal diagnosis of fetal hemivertebra]** [in Greek].

**Varras M.**, Akrivis Ch., Plis Ch., Karadaglis S., Ladopoulos I., Antoniou N.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 52, number 27.

**34. [Emergency obstetric hysterectomy in two tertiary centers]** [in Greek].

**Varras M.**, Akrivis Ch., Karadaglis S., Kanellopoulos N., Antoniou N., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 69, number 46.

**35. [Extraskkeletal chondroma of the fallopian tube associated with tubal ectopic pregnancy]** [in Greek].

**Varras M.**, Akrivis Ch., Tsoukalos G., Plis Ch., Karadaglis S., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 34, number 8.

**36. [Newborn transfers from "TZANEIO" general hospital of Piraeus to intensive neonatal care units]** [in Greek].

**Varras M.**, Karadaglis S., Kanellopoulos N., Akrivis Ch., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 44, number 19.

**Abstract:**

**Purpose:** The aim of this study was to determine the rates and causes of neonatal transfers from a Tertiary Obstetrics and Gynecology Department of Attica to neonatal intensive care units of Attica. **Methods:** In this retrospective study we examined the number and causes of neonatal transfers from Obstetrics and Gynaecology Department of "TZANEIO" General Hospital of Piraeus to intensive neonatal units of Attica during the period 1994-2003. The data were taken from the book of transfers of the labor ward. **Results:** During the study period 335 infants were transferred from a total of 8,735 births (3.83%). The annual rates of transfers ranged from 2.9% to 4.66% without presenting specific annual variances. The main causes for transfers were prematurity (134 transfers, 40%), respiratory causes (213 transfers, 33.72%), jaundice (19 transfers, 5.67%), sloth, drowsiness (13 transfers, 3.88%), infections (10 transfers, 3.35%), weakness for feeding, vomiting (9 transfers, 2.68%), hypoglycemia (6 transfers, 1.79%), cyanosis (4 transfers, 1.19%), heart

disease (3 transfers, 0.89%) and other causes such as cleft palate, meningomyelocele, incomplete occlusion of the scalp etc. (13 transfers, 3.88%). **Conclusions:** The transfer of newborns in intensive neonatal units represented 3.83% of births. The majority of the cases for the transfers was the prematurity and respiratory causes (74%).

**37. [Uterine rupture at the scar of previous cesarean section during induced second trimester pregnancy termination in the management for fetal abnormalities using misoprostol] [in Greek].**

**Varras M.,** Karadaglis S., Akrivis Ch., Plis Ch., Tsoukalos G., Ladopoulos I.

**Presentation:** 5<sup>th</sup> Greek National Conference of the Greek Society of Maternal Fetal Medicine, 16-18 May 2008, Volos

**Publication:** Book of Abstracts, page 71, number 47.

**Abstract:**

**Introduction:** Few cases have been published in the international literature on the use of misoprostol for the second trimester termination of pregnancy in uterus with previous scars. **Case:** We present the case of a 23 year old pregnant woman with a uterine scar from previous low transverse cesarean delivery, who was admitted to hospital at the 22<sup>nd</sup> gestational week for pregnancy termination due to multiple abnormalities of the fetus. 800 micrograms of misoprostol were administered vaginally every 4 hours until the beginning of regular uterine contractions. After the third dose, occurring vaginal bleeding and uterine contractions became intense. The woman miscarried completely 2 hours after the third dose. Uterine rupture diagnosed in the preceding section when caesarean finger control the die under general anesthesia. The patient underwent emergency laparotomy and the uterus was sutured at the position of rupture. **Conclusions:** The use of misoprostol in the second trimester of pregnancy in a woman with a previous uterine scar can cause intense contractions, which may lead to uterine rupture at the site of the scar.

**38. [Study of expression levels of Oct-4, DAZL and survivin genes in human luteinized granulosa cells of women undergoing ovulation induction for IVF or ICSI end embryo transfer: clinical correlations] [in Greek].**

**Varras M.,** Polonifi K., Griva Th., Mavrogianni D., Bletsas R., Dinopoulou V., Matzourani M., Stefanidis K., Loutradis D.

**Presentation:** 12<sup>th</sup> National Greek Congress of Obstetrics and Gynecology, 17-20 May, Thessaloniki, Greece

**Publication:** Book of Abstracts, pages 43-43.

**Award for the best study of the 12<sup>th</sup> National Greek Congress of Obstetrics and Gynecology from the Greek Society of Obstetrics and Gynecology**

**Abstract:**

**Objective:** To determine the incidence of expression of SURVIVIN, OCT-4 and DAZL in human granulosa cells during ovarian stimulation in women with normal FSH levels, undergoing IVF or ICSI. To investigate the presence or not of stem cells in follicular granulosa cells. To test if the levels of genes expression in granulosa cells could indicate number of oocytes retrieved, oocyte quality and developmental

competence. To discover any correlation of genes expression with the clinical parameters of patients, the efficacy of ovulation and the outcome of IVF or ICSI. To explore if the examined genes could be molecular prognostic markers for embryo development to increase the chance of a successful pregnancy with assisted reproductive technologies by optimizing oocyte and embryo selection. **Design:** Prospective Clinical research study of patients undergoing IVF or ICSI. **Setting:** IVF Center, University Department of Obstetrics and Gynecology, "Alexandra" General Hospital, Athens and Research Laboratory, First Department of Internal Medicine, "Laiko" General Hospital, Athens, Greece. **Patient(s):** Women undergoing oocyte retrieval for IVF or ICSI after ovulation induction with gonadotropins gave written consent to participate in this study. Twenty nine women were examine for SURVIVIN gene expression and twenty one for OCT-4 and DAZL gene expression. The causes of infertility were male or tubal factor. **Intervention(s):** Controlled ovarian hyperstimulation, serum hormone level measurements, ultrasonographic scanning of ovarian follicles, oocyte retrieval after hCG administration and embryo transfer were performed. Cumulus–oocyte complexes were denuded separately and the cumulus cells were analyzed for each patient separately. In all cases three embryos were transferred. **Material and Methods:** All of the patients were stimulated with standard GnRH analogue-recobinant FSH protocol. Total RNA was extracted from granulosa cells and was reverse transcribed into cDNA using specific designed primers for SURVIVIN, OCT-4 and DAZL. SURVIVIN mRNA, OCT-4 mRNA and DAZL mRNA in human granulosa cells were detected by RT-PCR using fluorescent probes. To determine the steady amount for SURVIVIN, OCT-4 and DAZL mRNA levels in granulosa cells, a quatitative competitive PCR (QC RT-PCRE) was developed. The number of trancripts of studied target genes was normalized according to the number of trancripts of the internal standard genes ABL and G6PD. The respective quatitative ratio was determined by the density of each target to the internal standard: Survivin mRNA / ABL mRNA, OCT-4 mRNA / G6PD mRNA and DAZL mRNA / G6PD mRNA. **Main Outcome Measure(s):** The expression rates of SURVIVIN, OCT-4 and DAZL of granulosa cells surrounding the oocytes were determined in the studied patients. Many variables were analyzed: age, BMI, infertility causes, infertility duration, previous IVF/ICSI cycles, serum concentrations of FSH, LH, progesterone, AMH at the beginning of the menstrual cycle, serum PRL levels, as measured during one of the previous six months, serum 17b-estradiol levels on the 5th day of FSH treatment and on the day of hCG, duration of stimulation, total FSH dose used for ovarian stimulation, ovarian response, oocyte maturity, embryo quality (grade), good quality embryos score, fertilization and pregnancy rates. **Results:** ABL and SURVIVIN mRNA was detected in the granulosa cells in 93.1% (27/29). The median of SURVIVIN mRNA /ABL mRNA was 0.45 with intra-quarteral range from 0.22 to 2.94. The quatitative ratio of Survivin mRNA was significantly lower in normal women (male infertility factor) compared to women with tubal infertility factor ( $p=0.007$ , Wilcoxon ran-sum test). G6PD and OCT-4 mRNA was detected in the granulosa cells in 47.6% (10/21). The median of OCT-4 mRNA / G6PD mRNA was 1.75 with intra-quarteral range from 0.10 to 98.21. The OCT-4 mRNA expression was statistically significant correlated with the number of oocytes retrieved; when the OCT-4 mRNA expression was higher then more than six oocytes were retrieved ( $p=0.037$ , Wilcoxon rank-sum). No detection of DAZL mRNA was found in granulosa cells. The levels of expression of

OCT-4 were not connected with the levels of expression of SURVIVIN (Spearman's  $\rho=0.429$ ,  $p=0.289$ ). There was no additional statistically significant correlation between the levels of SURVIVIN or OCT-4 expression and the estradiol levels or the dosage of FSH for ovulation induction or the number of dominant follicles aspirated or the clinical pregnancy rates respectively. There was no statistically significant correlation between the levels of SURVIVIN expression and the number of retrieved oocytes. No association was found between the presence or absence of OCT-4 mRNA expression in granulosa cells and the ovarian response to gonadotropin stimulation. Also, no influence on pregnancy was observed between presence and absence of OCT-4 mRNA expression in granulosa cells or accordingly to its expression levels.

**Conclusions:** High levels of SURVIVIN mRNA expression in luteinized granulosa cells in cases with tubal infertility seems to be observed for possible protection from follicular apoptosis. A subpopulation of patients with low levels of SURVIVIN mRNA in granulosa cells might benefit with ICSI treatment to bypass possible natural barriers of the sperm-oocyte interactions. The expression of OCT-4 mRNA, which is a typical stem cell marker and the absence of expression of DAZL mRNA, which is a typical germ cell marker, both increase the indications that a subpopulation of luteinized granulosa cells in healthy ovarian follicles (47.6%) consists of stem cells which are not originated from primordial germ cells. Increased number of oocytes retrieved seems to correlate to higher levels of OCT-4 mRNA expression. Oct-4 expression in luteinized granulosa cells seems not to be required for protection from apoptosis.

#### **PARTICIPATION IN BOOKS, BOOK CHAPTERS, CD-ROMs**

1. Invaluable assistance in the writing of the scientific book in the subject of Obstetrics and Gynecology **"News in Obstetrics and Gynecology"**, D.I. Aravantinos, 1996. Thanks of Professor D.I. Aravantinos to Protopoppos A., **Varras M.**, Zafiriou S.

2. Co-author in Book Chapter in the subject of Obstetrics and Gynecology.

**Book Chapter: "Molecular Biology of Gynecological Cancer"**

**In the Book: "Gynecological Oncology"**, Pectasidis D., M.A. Dimopoulos (eds), Publisher "P.Ch. Paschalidis", 2001.

3. Co-author in the book **"Obstetrics–Gynecology"**, Agency Office of Educational Books, Greek Ministry of Education, 1999, following an open tender.

**Varras M.**, Theodori-Lacafosi V., Zourbaki A. Number of pages: 190.

The book is used for the teaching in Technical Vocational Education of Greece, Second Circle for Health and Welfare.

4. Participation in creating scientific CD-ROMs (Multimedia).

Participation in writing and creating CD-ROM (Multimedia) of **Laparoscopy in Gynecological Surgery** in collaboration with Adam Magos and Medical Illustrator Department of the Royal Free Hospital, London, UK, 1999. **"Gynaecological Endoscopic Surgery: Movies"**, CD-ROM, 2000 - A compilation of hysteroscopic and laparoscopic surgery for delegates attending the "Hands On"

Gynaecological Endoscopy Skills Workshop at the Royal Free Hospital, London, U.K.  
Movies edited by Adam Magos, Nikolaos Bournas and **Michael Varras**.

The CD-ROM includes sort video clips that illustrate the surgical techniques of the following interventions:

**A. Hysteroscopy**

- A1. Diagnostic Hysteroscopy
- A2. Hysteroscopic Endometrial Anesthesia
- A3. Hysteroscopic Polypectomy
- A4. Hysteroscopic Fibrectomy
- A5. Hysteroscopic Plastic Surgery of the Uterus (hysteroscopic removal of uterine septum)
- A6. Hysteroscopic Endometrial Adhesiolysis
- A7. Myometrial scoring
- A8. TCRE

**B. Basic Laparoscopic Surgery**

- B1. The technique for creating Pneumoperitoneum
- B2. The technique for entry of the laparoscope from the Palmer's point
- B3. The technique for creation ancillary ports
- B4. The technique for tissue removal through the peritoneal cavity using Kocher forceps.
- B5. The technique for laparoscopic sac removal from the peritoneal cavity through posterior colpotomy
- B6. The technique using electronic morcellator

**C. The technique for laparoscopic tissue suturing**

- C1. The technique for creating Roeder's laparoscopic knot
- C2. The technique for creating Weston's laparoscopic knot
- C3. The technique for generating laparoscopic knot in cases of abdominal wall adhesions
- C4. Laparoscopic needle suture with extracorporeal tie
- C5. Laparoscopic needle suture with intracorporeal tie

**D. Laparoscopic Surgery: uterine adnexae**

- Δ1. Laparoscopic surgery for ovarian cyst
- Δ2. Laparoscopic surgery for ovarian cyst into a bag
- Δ3. Laparoscopic drainage of ovarian cyst into a bag
- Δ4. Laparoscopic ovarian drilling
- Δ5. Laparoscopic salpingo-neostomy
- Δ6. Laparoscopic salpingotomy for ectopic pregnancy
- Δ7. Laparoscopic salpingectomy for ectopic pregnancy
- Δ8. Laparoscopic salpingo-oophorectomy

**E. Laparoscopic Surgery: uterus and vaginal stump**

- E1. Laparoscopic fibrectomy
- E2. Laparoscopically assisted vaginal hysterectomy
- E3. Laparoscopic sacrocolpopexy
- E4. Laparoscopic pelvic lymphadenectomy

5. Zoe Iliodromiti, Charalampos Grigoriadis, Nikolaos Vrachnis, Charalampos Siristatidis, **Michail Varras** and Georgios Creatsas. **“Association of Meconium**

**Stained Amniotic Fluid with Fetal and Neonatal Brain Injury**", In: **Neonatal Care**, Deborah Raines and Zoe Iliodromiti (Eds.), ISBN: 978-953-51-0692-0, InTech, 2012.

## **AWARDS**

- From the **Greek Society of Obstetrics and Gynecology**, Member of the FIGO, the physician **Dr Michail Varras** and partners were awarded on 26 of November 1994 with the Honorary Diploma Award **in memory of "Ioannis Mantalenakis"** and 300,000 greek drachmas prize money for the best free communication to the **6th National Congress of Obstetrics and Gynecology, Athens, Greece** entitled **"Activation of the oncogene K-ras in tumors of the endometrium"**.
- From the **Greek Society of Obstetrics and Gynecology**, Member of the FIGO, the physician **Dr Michail Varras** and partners were awarded on 20 of May 2012 under the **12th National Congress of Obstetrics - Gynecology, 17-20 May 2012, Thessaloniki, Greece** with the Award and 500 euros prize money for the best free communication of the conference entitled **"Study of the expression levels of genes Oct-4, DAZL, and survivin in human follicular luteinized granulosa cells of the ovaries, in women undergoing ovulation induction for *in vitro* fertilization (IVF) or ICSI (ICSI) and embryo transfer: clinical correlations"**.