

Kurjak A, Stanojević M, Azumendi G, Carrera JM. The potential of four-dimensional (4D) ultrasonography in the assessment of fetal awareness. J Perinat Med. 2005;33:46-53.

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The aim of the study was to observe different expressions and movements of a fetal face during investigation of fetal behavior in the second and the third trimester of normal pregnancies, as a probable manifestation of fetal awareness. Over a 6-month period a study was conducted in three centers in Zagreb, Croatia and in Barcelona and Malaga, Spain. Women with singleton pregnancies (16-33 weeks) who were referred for ultrasound check-up for determination of gestational age, suspicious fetal malformations, polyhydramnios, and/or the assessment of biophysical profile or other possible pathology, were assigned to the study. After regular two-dimensional (2D) ultrasound assessment at an antenatal clinic, pregnant women were offered the possibility of undergoing 4D ultrasound examination if the fetus and the mother were considered "normal", i.e., if ultrasound and clinical assessment were uneventful. If the newborn delivered at term had 1- and 5-min Apgar scores of 7 and 10, respectively, and if the newborn was considered "term and normal" (normal spontaneous activity, normal posture and tone, and presence of some primitive reflexes) at the first and subsequent regular check-ups, the inclusion criteria were deemed to have been met. A Voluson 730 Expert system with a transabdominal 5-MHz transducer was used for 4D ultrasonography. Movements of the following fetal face structures were analyzed: forehead, brows, nasal soft tissue and nasolabial folds, upper lip, oral cavity and tongue, lower lip and chin, eyelids and eyes, mouth and mouth angles, and facial expression. 4D ultrasonography allowed in utero observations of fetal facial expressions such as smiling, yawning, and swallowing. The quality of 4D depiction of fetal facial expressions increased with gestational age. The frequency of fetal facial expressions such as yawning ranged from 1 and 6 with a median of 1.5 per 30-min observation period; smiling ranged from 2 and 8 with the median of 2; tongue expulsion ranged from 2 to 6, median 3; mouth and eye squeezing ranged from 5 to 10, median 6; scowling ranged from 1 to 3, median 0.5; and isolated eye blinking ranged from 4 to 12 with a median of 5. This study shows the ability of 4D sonography to depict different facial expressions and movements, which might represent fetal awareness. Nevertheless, long, precise and thorough observation of fetal faces by 4D sonography was hampered as the images were only near real-time. Thus, the authors were only able to study

the quality and not the quantity of facial movement patterns.

Bauman R, Vujisić S, Tripalo A, Akšamija A, Hafner D, Emedi I, et al. Influence of hormonal stimulation on in vitro fertilization/embryo transfer outcome. Eur J Obstet Gynecol Reprod Biol. 2005;119:94-102.

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The aim of this study was to compare efficacy and efficiency of ovarian stimulation therapy. Retrospective study compares ovarian response as number of retrieved oocytes, fertilization rates, endometrial patterns, number of pregnancies and pregnancy rates to different stimulation protocols. The least number of cancelled cycles was in long protocols with buserelein. There was no difference in overall number of retrieved oocytes between the rFSH and HMG protocols, but 75% of the patients undergoing both protocols had higher number of oocytes after rFSH. The highest pregnancy rate (35.13%) was with rFSH. There was no statistical correlation between endometrial pattern and type of protocol used. Data showed the 9 mm cut-off value for endometrial thickness, and RI=0.58 for subendometrial blood flow between the pregnant and non-pregnant group of patients. Nitriderm patches significantly decreased ($P<0.05$) subendometrial RI of the patients with impaired uterine perfusion, increased endometrial thickness and achieved better morphology. These findings demonstrate that rFSH alone and in long protocol gives better results in wide patient population. Nitriderm patches seem to have good impact on pregnancy rate, but further studies are necessary before making any statements.

Ivančić J, Gulija TK, Forčić D, Baričević M, Jug R, Mesko-Prejac M, et al. Genetic characterization of L-Zagreb mumps vaccine strain. Virus Res. 2005;109:95-105.

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Eleven mumps vaccine strains, all containing live attenuated virus, have been used throughout the world. Although L-Zagreb mumps vaccine has been licensed since 1972, only its partial nucleotide sequence was previously determined (accession numbers , and). Therefore, the authors sequenced the entire genome of L-Zagreb vaccine strain (Institute of Immunology Inc.,

Zagreb, Croatia). In order to investigate the genetic stability of the vaccine, sequences of both L-Zagreb master seed and currently produced vaccine batch were determined and no difference between them was observed. A phylogenetic analysis based on SH gene sequence has shown that L-Zagreb strain does not belong to any of established mumps genotypes and that it is most similar to old, laboratory preserved European strains (1950s-1970s). L-Zagreb nucleotide and deduced protein sequences were compared with other mumps virus sequences obtained from the GenBank. Emphasis was put on functionally important protein regions and known antigenic epitopes. The extensive comparisons of nucleotide and deduced protein sequences between L-Zagreb vaccine strain and other previously determined mumps virus sequences have shown that while the functional regions of HN, V, and L proteins are well conserved among various mumps strains, there can be a substantial amino acid difference in antigenic epitopes of all proteins and in functional regions of F protein. No molecular pattern was identified that can be used as a distinction marker between virulent and attenuated strains.

Turk N, Kušec R, Jakšić B, Turk Z. Humoral SPARC/osteonectin protein in plasma cell dyscrasias. *Ann Hematol.* 2005;84:304-10.

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The matricellular protein SPARC (secreted protein acidic and rich in cysteine)/osteonectin was determined in patients with multiple myeloma and related disease to assess the hypothesized role of SPARC as a possible marker of tumor burden and disease progression. Soluble SPARC was measured by competitive enzyme-linked immunosorbent assay (ELISA) in plasma of 42 patients, including sequential measurements in individual patients, and in 20 healthy controls. SPARC values were heterogeneous in multiple myeloma patients showing a decline from baseline levels recorded in controls (456 ± 195 vs 600 ± 63 ng/ml, $P=0.00023$). A SPARC showed a significant positive correlation with platelet count ($r=0.72$, $P=0.000000$, $n=42$), hemoglobin ($r=0.52$, $P=0.00037$, $n=42$), and IgG level ($r=0.43$, $P=0.0085$, $n=42$) and negative correlation with beta₂-microglobulin ($r=-0.46$, $P=0.0023$, $n=42$), aspartate aminotransferase (AST) ($r=-0.42$, $P=0.0061$, $n=41$), interleukin (IL)-6 ($r=-0.41$, $P=0.008$, $n=42$), lactate dehydrogenase (LDH) ($r=-0.36$, $P=0.02$, $n=41$), and percentage of plasma cells in bone marrow aspirate ($r=-0.34$, $P=0.029$, $n=42$). No correlation was found between SPARC and "M" component or disease stage. Investigations performed during the course of disease, including sequential measurements in individual patients, showed a trend to downregulation by disease progression, with the lowest level recorded in the terminal stage (217 ± 107 ng/ml, $n=11$). Patients with established osteolytic lesions had lower plasma SPARC at diagnosis (309 ± 197 vs 581 ± 293 , $P=0.021$), which correlated with osteocalcin by disease progression ($r=0.31$, $P=0.026$). The results of this pilot study revealed abnor-

malities in the level of humoral SPARC in multiple myeloma and an overall trend to downregulation in the advanced stage of the disease. The regulation of SPARC seems to be opposite to the markers of tumor burden and of aggressive multiple myeloma phenotype.

Skodlar J, Štimac D, Majerić-Kogler V, Doughty H, Sibinga CS. The use of a World Health Organization Transfusion Basic Information Sheet to evaluate transfusion practice in Croatia. *Vox Sang.* 2005;89:86-91.

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The aim of this study was to assess the feasibility of using the World Health Organization (WHO) Transfusion Basic Information Sheet as a bedside tool for data collection and assessing transfusion practice. A prospective 6-month audit of all transfusion episodes using the tool. Eight hundred and twenty-two forms were completed, capturing data on 59.7% of transfusion episodes. Completion of data fields was >80%, except for the clinician's transfusion targets that were documented in only 58.5% of cases. Twenty per cent of patients received single red cell unit transfusions. The Basic Information Sheet can be incorporated into bedside clinical practice. We have identified the need to encourage clinicians to determine and document their transfusion targets before prescribing blood components.

Likić R, Dušek T, Horvat D. Analysis and prospects for curricular reform of medical schools in Southeast Europe. *Med Educ.* 2005;39:833-40.

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The aim of this study was to analyse the curricula of 16 medical schools in 6 countries in Southeast Europe in order to establish a prevailing standard curriculum against which a prospective curriculum reform could formulate its objectives. Curricular information was gathered from a questionnaire sent via e-mail to the respective medical schools. The data collected ranged from the numbers of enrolled students to a breakdown of courses with distribution of instruction hours for certain teaching formats. For easier comparison the courses were clustered into 5 groups: pre-clinical, clinical, public health, liberal arts and electives. Belgrade has the highest number of undergraduate students, while Mostar has the lowest. Novi Sad, Foca/Srbijne, Zagreb, Split, Sofia, Ljubljana and Mostar have more than 5000 instruction hours, but Sarajevo lags behind with 4005 hours. Anatomy dominates the course load in Year 1, ranging from a share of 18.4% in Sofia to 11.3% in Novi Sad. Physiology dominates Year 2, ranging from 16.8% in Rijeka to 8.9% in Split, whereas in Year 3 the dominating course is pathology, reaching a peak of 13.7% in Sarajevo. Sofia has the highest number of class hours of clinical courses. The predominant public health courses are social medicine, family medicine and medical ecol-

ogy. Medical English is taught at all medical schools (as electives in Ljubljana and Rijeka). There is considerable potential for curriculum improvement in the region. Teacher training, student participation, the definition of core competencies and the introduction of new methodologies should all be implemented in the process.

Mitrečić D, Huzak M, Ćurlin M, Gajović S. An improved method for determination of gene copy numbers in transgenic mice by serial dilution curves obtained by real-time quantitative PCR assay. J Biochem Biophys Methods. 2005;64:83-98.

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Precise characterization of transgene insertion is necessary for phenotype interpretation of transgenic animals. To check for the presence of deletions, estimate the number of inserted transgene copies, and in addition, identify the zygosity of transgenic mice, gene copy numbers were determined by real-time quantitative PCR. Instead of correlating tested samples to a single relative standard curve, serial dilution curves were constructed for every mouse sample. A novel statistical approach was designed in which mice with the same copy number were characterized by the adjusted group mean and standard deviation common to the target sequence. This enabled the authors to characterize the variability of the obtained results, statistically compare different groups of mice and estimate precision and limits of the applied method.

Matijević R, Grgić O. Predictive values of ultrasound monitoring of the menstrual cycle. Curr Opin Obstet Gynecol. 2005;17:405-10.

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This paper summarizes the current knowledge about ultrasound scanning values in monitoring the structural and functional changes of the uterus and ovaries during the menstrual cycle. Recent findings challenged the views that ovulation is more frequently right sided, with recent data suggesting that ovulation occurs randomly. A

'follicular wave phenomenon', providing a new model for ovarian function during the menstrual cycle, has been described. Follicular development occurs in a wave-like fashion and women with two waves have earlier endometrial development due to earlier increase of the dominant follicle estrogen production. Myometrial contractions during menstrual cycle should be considered in the assessment of endometrial thickness. Uterine-ovarian arterial blood flow impedance is important in understanding the normal physiology of the menstrual cycle and may be of use in assisted conception protocols. At present, ultrasound scanning has an important role in noninvasive assessment of endometrial and ovarian cyclical changes and may be of particular importance in assisted conception procedures. Further work is likely to help in understanding its full diagnostic potential.

Ristić S, Lovrečić L, Brajenović-Milić B, Starčević-Čizmarević N, Jazbec SS, Sepčić J, et al. Mutations in the hemochromatosis gene (HFE) and multiple sclerosis. Neurosci Lett. 2005;383:301-4.

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In the present study the authors have investigated whether HFE gene polymorphism may play a role in the disease process of Croatian and Slovenian MS patients and their potential genetic susceptibility to MS. They genotyped 314 MS patients and 400 healthy controls for the C282Y and H63D mutations by polymerase chain reaction/restriction fragment length polymorphism (PCR-RFLP) analysis. The results showed no significant differences in the distribution of the two mutations between MS patients and controls, suggesting that HFE polymorphisms do not contribute to the susceptibility to MS. Also, there was no significant correlation between HFE polymorphism and the disease progression index. However, the authors observed that MS patients carrying the mutant C282Y allele exhibited earlier onset of disease symptom relative to other genotypes, but this observation warrants further study in a larger series of MS patients.