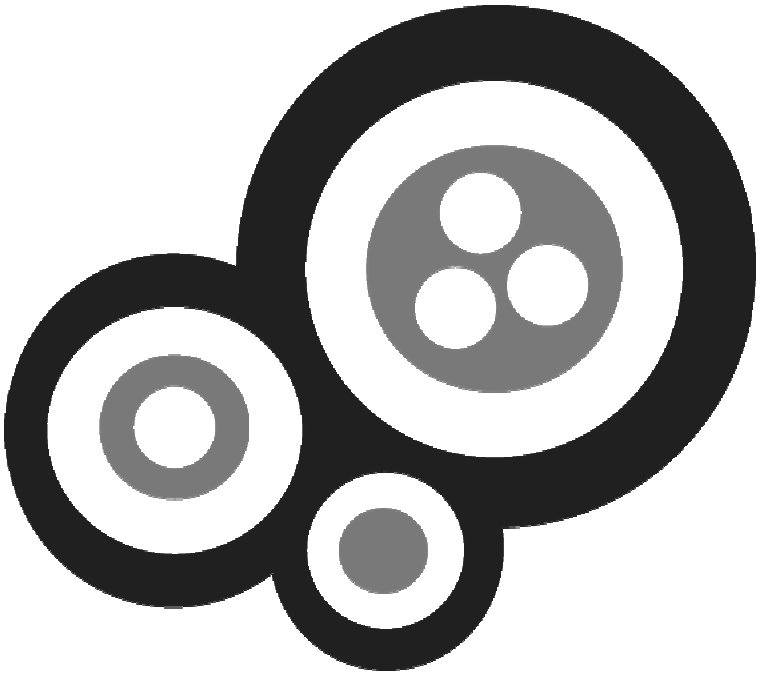

BREAKOUT 7

PRENATAL SCREENING AND DIAGNOSIS

Moderators:
Janos Szabo – Hungary
Gioacchino Scarano – Italy

ANTENATAL SCREENING FOR FETAL ABNORMALITIES IN HUNGARY

Janos Szabo

Department of Medical Genetics, University of Szeged, Szeged, Hungary

Prenatal diagnosis of *fetal chromosomal abnormalities* started in Hungary by applying amniocentesis in the late 1970s and chorionic villus sampling in the early 1980s being among the first countries in the world introducing these techniques.

In the presence of only a weak govermental support the motor of the development was mainly the personal ambition and scientific enthusiasm with an outstanding activity showed by obstetricians, geneticists and pediatricians devoted to prenatal diagnosis. The introduction of genetic counseling and prenatal screening methods and scientific cooperation with western world was the fructification of their activity.

Non-invasive screening for *fetal structural abnormalities* commenced in the early eighties by ultrasound and maternal serum alpha-fetoprotein (MS-AFP) determination.

The discovery of the correlation between increased *fetal nuchal translucency* and chromosomal trisomies in this country and its practical application outrun the introduction of maternal blood tests, which was introduced only in some regions and mainly the by the private sector.

The establishment of the Hungarian Society of Ultrasound in Obstetrics and Gynecology was the first step to official ultrasound education, which led to A, B, C level of qualification depending on training, experience and scientific activity.

A continuous development could be observed regarding *ethical principles* in prenatal screening which developed from paternalism through nondirective and to interpretative counseling concept.

Up to now there is no nationwide unified concept for screening of fetal defects. In addition to the university based governmental screening, a growing number of private companies are offering their business based service.

As in other European countries the basic technique is the ultrasound screening. Interest is growing in early detailed fetal ultrasound at the time of nuchal translucency thickness assessment since qualified ultrasound examination provides not only chromosomal risk assessment, but gives a “holistic approach” to the fetus.

There are many tasks ahead us: 1. selection and introduction of the most sensitive novel techniques, 2. continuous theoretical and 3. practical training and education, 4. refreshing guidelines by the clinical genetic board, 5. quality control.

IS IT TIME TO CHANGE FROM CLASSICAL KARYOTYPING TO RAPID TESTING IN PRENATAL DIAGNOSIS?

Karolina A. Pesz, I. Laczmanska, J. Kozlowska, I. Makowska, R. Slezak, R. Smigiel, A. Stembalska, M. M. Sasiadek

Wroclaw Medical University, Chair and Department of Genetics, Wroclaw, Poland

Classical karyotyping in prenatal diagnosis has been the golden standard for many years. However, the waiting period of 2-3 weeks before the results are issued leads to the increase in pregnant women's anxiety and also to the delay in the decision making of continuation or termination of the aneuploid pregnancy.

Development of new rapid methods for prenatal detection of the most common aneuploidies (13, 14, 21, X and Y) raised the question of shifting from classical cytogenetics to novel techniques. The discussion is ongoing across Europe.

Therefore, we will present the results of RAPID-FISH analysis followed by classical karyotyping which was performed on 363 amniotic fluid samples obtained from pregnant women referred for invasive testing due to maternal age, positive results from non-invasive screening (including ultrasound abnormalities) and maternal anxiety.

The time needed to obtain the RAPID-FISH result was 2-5 days compared to the average 3 weeks needed to obtain the full karyotype. Compliance of RAPID-FISH with karyotyping was observed for both normal and 34 aneuploidic pregnancies. However, in 6 cases classical cytogenetic analysis revealed chromosomal structural aberrations (3 balanced and 3 unbalanced) not possible to detect by fluorescence hybridisation *in situ* used for prenatal diagnosis. Indications for invasive testing and possible pregnancy outcomes of those five cases were analysed.

Concluding, our results confirm the thesis that in cases with high risk of aneuploidy (e.g. advanced maternal age) rapid aneuploidy detection technique such as RAPID-FISH is of high utility. Therefore, indications for classical karyotyping and rapid testing should be reconsidered dependent on the ultrasound examination. RAPID-FISH should be implemented as routine in pregnancies with high risk of aneuploidy whereas classical karyotyping should be performed when chromosomal structural abnormalities are suspected.

PRACTICAL ASPECTS OF DOWN'S SYNDROME SCREENING – THE GENERAL INTRODUCTION OF COMBINED TEST

Eszter Skriba, Zoltan Merhala

Magzati Diagnosztikai Központ (Fetal Diagnostic Centre), Budapest, Hungary

Supported by data, we give an overview on the methodology of Down's Syndrome screening and on the conditions for applying the different kinds of screening tests. We compare the first trimester Combined Test, the second trimester Quadruple Test and their complex analysis, called Integrated Test with respect to their performance on average negativity and average positivity and we emphasize on its practical importance. We present our data. We performed 3388 Quadruple Test between 1999 and 2008. We detected 66% of the Down's Syndrome affected pregnancies /sensitivity/ with a 9.2% FPR /specificity/ used risk cut-off 1:250. The average age of the women attending the screening was 32 years, 28% of them were above 35 years of age, which is more then double the rate of the pregnant above 35. Between 2003 and 2008 we performed 3065 Integrated Tests. By the Integrated Test, 100% of Down's Syndrome affected were detected /sensitivity/ with a 2.5% specificity, used risk cut-off 1:150. The average maternal age was 33. 37% of them were above 35 years of age. Our results are matching with earlier published performace of the different test methods.

In the frame of the presentation, we would like to introduce our new concept of mass screening by Combined Test to be offered for the regional antenatal care centres free of charge by our organization.

GENETIC COUNSELING AS A KEY FOR BIRTH DEFECTS PREVENTION

Habiba Chhabouni-Bouhamed, Myriam Chaabouni, Imen Chelly, Lilia Kraoua, Ines Ouertani, Faouzi Maazoul

Department of Genetics, Tunis, Tunisia

Genetic counseling remains the best and the most efficient action for genetic diseases prevention. Based on families' education, and sometimes followed by prenatal or preimplantation diagnosis, genetic counseling is relevant by reducing the incidence of hereditary and congenital disorders. The development of medical care, the accumulation of laboratory techniques and the legality of pregnancy termination will help largely to decrease the severity and the frequency of inherited diseases.

In daily practice we are sometimes surprised by parents' attitude. After genetic counseling, why do parents decide to stop reproduction despite the availability of prenatal testing or the absence of recurrence risk? While, some other parents at very high risk continue to have children. To reply to such questions we surveyed during three years couples who were referred to the genetic center for genetic counseling. We considered only couples at risk of birth defects affected children. We evaluated the impact of genetic counseling on parents' attitude by analyzing two parameters, the occurrence of pregnancies and the acceptance of prenatal screening and prenatal diagnosis. These parameters were correlated to parents' characteristics: age, socioeconomic situation, education level; to the number and children health status and to the kind and severity of the disease. We analyzed simultaneously the same parameters in the group of couples who were referred for prenatal diagnosis during this period. The aim of the presentation is to evaluate the real impact of genetic counseling and prenatal diagnosis on genetic diseases prevention in an Arab Muslim country and to determine how to increase the acceptability of the role of genetic counseling in welfare family.

POLISH COLLECTION OF CHROMOSOMAL TRANSLOCATION

Alina T. Midro and Polish Group for Chromosome Translocation Evaluation

Department of Clinical Genetics, Medical University Bialystok, Poland

Despite of availability of prenatal cytogenetic services the parents with balanced chromosome translocation should be informed about likelihood for chromosome imbalance leading to miscarriage, stillbirth or viable handicapped baby. This probability changes from translocation to translocation and empirical data are b necessary to obtain risk figures. The degree of the accuracy of the risk figures estimation depends on the number of informative pregnancies conceived in the case of RCT parental carriership, the precision of identification of breakpoint position in the involved chromosomes. Additionally the UPD effect on particular chromosome regions and the X chromosome inactivation spreading to the autosomal segment and/or generating functional imbalance in particular sets of RTC should be considered. Aim of organizing of Polish Collection of Chromosome Translocations was to obtain empirical data of individual RCT carriers to improve genetic counselling and to collect clinical observations connected with chromosomal changes as a valuable resource for locating the disease gene. We collected data about 700 pedigrees and use them for genetic counselling will be presented.