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Genetic risk assessment in women over 35: natural pregnancies compared to assisted reproductive technology pregnancies. M. Pearson, J. Neidich. Stanford University, CA.

The number of women of advanced maternal age (AMA), as well as the number of AMA women who utilize assisted reproductive technology (ART), has increased, yet very few studies have been conducted to understand their experience. The purpose of this study was to examine the differences in genetic risk assessment and decision-making between two groups of AMA women: those who had natural pregnancies and those who had ART pregnancies. The main hypothesis of the study was that AMA women with natural pregnancies would be more likely to elect prenatal diagnostic procedures than would AMA women with ART pregnancies because the latter would have greater anxiety about the risk of miscarriage. The alternative hypothesis was that the ART experience would desensitize women to invasive procedures, leading them to view prenatal diagnostic procedures as low-risk.

The method used for study was a questionnaire, administered over a 7-month period of time at the Stanford University Hospital Genetic Counseling Clinic. Case study interviews were later conducted to obtain detailed information about individuals' experiences as women of advanced maternal age.

The data indicated that the use of assisted reproductive technology did not shape the women's decision whether to undergo prenatal diagnostic testing, but the sample size was very small ($p > .05$). Trends in questionnaire and interview responses suggested that maternal age and the associated risk of fetal abnormality were the predominant factors shaping the risk assessment of the women in the study, not the use of ART. The alternative hypothesis, that ART may lead to desensitization toward prenatal diagnostic procedures, was supported by the interviews.

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Preconceived Ideas about Second Trimester Screening: a Guide for Counseling

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Women of 10 -14 weeks of pregnancy who were participating in a study of first trimester screening for chromosomal abnormalities were invited to complete a questionnaire. This examined their knowledge about the triple test, perception of risk and views on screening. The response rate was 70.3% (270/384). The mean age of responders was 34.2 years and 47% (127/270) had a child already. Of those between 35 and 39 years 47.6% (40/84) planned to use the triple test to decide about amniocentesis as did 6.9% (2/29) of those of 40 years or more and 50.7% (136/268) of responders overall. When asked what they would do if the fetus had Down syndrome 22.0% (58/264) said they would terminate the pregnancy, 22.3% (59/264) would continue and 55.7% (147/264) were uncertain. Almost half (47.9%; 126/263) of patients correctly identified the detection rate for the triple test as approximately 65%, 33% underestimated the detection rate and 19% overestimated it. When asked about the false positive rate, 13.0% (32/246) correctly identified it as 1 in 20, 16.7% said 1 in 50, 43% said 1 in 100 and 27.2% said 1 in 1000. Almost all responders (96.9%; 248/256) correctly answered that a woman with a low risk test result could have an affected baby. Over a third (34.4%; 88/256) were unaware that most women with a high risk result have a chromosomally normal baby. Women were asked to estimate their risk for Down syndrome. Responders estimated their risk to be less than half of the age related risk in 35% (89/266) of cases and overestimated it by at least two times in 13%. When asked how they considered their risk: 90% (135/150) under 35 years, 55.3% (47/85) between 35 and 39 years and 20.7% (6/29) of 40 years or more, considered themselves as being "low risk". In this group most responders planned to use the triple test but most were unsure what they would do with the information. Many perceived their risk to be lower than their age related risk. Almost all were aware that the test was not 100% sensitive but many overestimated the significance of a "high risk" result. They also underestimated the false positive rate. Emphasizing these points to women prior to screening may help alleviate some of the distress that is often experienced with false positive results.

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Low maternal serum estriol as a marker for steroid sulfatase deficiency. C.L. Stanislaw[1], R.C. Rogers[1], K. Stewart[1] and M.C. Phelan.[2] [1]Greenwood Genetic Center, Greenwood, SC and [2]T.C. Thompson Children's Hospital, Chattanooga, TN.

Maternal serum screening began in the early 1980's with the evaluation of alpha-feto-protein (AFP) levels to identify pregnancies at an increased risk for neural tube defects and later for Down syndrome. Elevated levels of AFP have been found to be markers for other conditions like gastroschisis, kidney abnormalities and placental bleeding. Maternal serum screening now includes hCG and estriol to increase aneuploidy detection, with estriol being added in the mid 1990's. Since that time many screening tests have shown abnormally low levels of estriol (≤0.10 MoM). These low values have been reported in association with anencephaly, Smith-Lemli-Opitz, fetal adrenal hypoplasia, high-dose corticosteroid therapy and steroid sulfatase deficiency. We report on 4 cases of very low estriol levels detected through maternal serum screening and referred to our center. The values were 0.02 MoM, <0.03 MoM, 0.06 MoM and 0.10 MoM. In all cases the mothers were found to be carriers of a microdeletion in the steroid sulfatase (STS) region at Xp22.3 by FISH analysis. All had affected sons. Three were detected by amniocentesis and one was tested after delivery. Three cases had a family history of very dry skin consistent with an X-linked recessive inheritance pattern. STS deficiency should be considered when counseling patients presenting with very low maternal serum estriol levels. STS deficiency or X-linked ichthyosis is characterized by dark scaly skin most prominent on the back, neck, face and extremities. Approximately 25% of affected males may develop mild corneal opacities. Carrier females may have mild symptoms. In an estimated 5% of cases, a more severe phenotype may be present resulting from a larger deletion and leading to a contiguous gene syndrome. Other conditions mapped to Xp22.3 include short statue, chondrodysplasia punctata, mental retardation, Kallmann syndrome and ocular albinism. Carrier testing and prenatal diagnosis are available. Testing can help elucidate the reason for low estriol levels and identify women at risk for prolonged labor and failure to dilate due to placental sulfatase deficiency. A detailed family history may assist in determining the risk of STS deficiency or a more severe contiguous gene syndrome.