297 **THE EFFECT OF INACCURATE GESTATIONAL AGE ESTIMATION ON THE MULTIPLE MARKER SCREENING TEST (MMST) FOR FETAL DOWN SYNDROME (DS).** *J. Owen, K. D. Wenstrom.* Dept. of OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: The MMST (Age, hCG, AFP, E_3) for fetal DS detection requires a precise estimate of gestational age (GA), because week-specific medians are used to convert each analyte concentration into a multiple of the median (MOM) prior to calculation of the DS risk. GA is determined by last menstrual period or by sonography if a discrepancy is discovered. Errors in GA estimation affect the combined risk of DS and can result in both false positive and false negative test results. However, the magnitude of these errors is unknown. We sought to quantify the error in risk assignment associated with GA inaccuracies.

STUDY DESIGN: Using our laboratory's week-specific analyte medians over the GA range 14-21 wks as a reference, we computed the Risk Error Factor in a multivariate Gaussian algorithm as the ratio of Estimated DS Risk:Actual DS Risk using GA Errors (Actual-Estimated GA) from −3 to +3 weeks. We also varied the baseline analyte values from .5 to 2.0 MOM in the algorithm to determine the effect of various analyte combinations on the Risk Error Factor. Linear regression was used to model the relationship between the derived Risk Error Factor and both the actual GA and baseline MOM values.

RESULTS: The mean Error ranged from a Factor of a 4-fold Risk *overestimation* to a two thirds Risk *reduction* at GA Errors of −3 and +3 wks respectively (Table). These risks were most pronounced earlier in gestation and diminished as the GA advanced ($p = .0001$). The hCG MOM was significantly related to the Risk Error Factor ($p = .0001$), while the E_3 MOM showed marginal significance ($p = .05$), and the AFP MOM was not significant ($p = .27$).

GA Error (wks)	−3	−2	−1	1	2	3
Mean Risk Error Factor	4.0	2.5	1.6	.67	.46	.33

CONCLUSIONS: Inaccurate GA estimation can dramatically alter the DS risk in the MMST. The magnitude of this effect provides a compelling argument for precise GA estimation (e.g. sonography) in women who choose this screening test.

298 **OPTIMIZING THE MULTIPLE MARKER SCREENING TEST FOR FETAL DOWN SYNDROME USING A PENTAVARIATE GAUSSIAN ALGORITHM.** *Owen J, Wenstrom KD, Boots L[x], Hsu J[x], Chu DC[x].* Departments of Ob/Gyn and Biostatistics, The University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To develop and test a pentavariate Gaussian algorithm to optimize both the sensitivity and the screen positive rate of the multiple marker test (MMST) for fetal Down syndrome (DS).

STUDY DESIGN: From our bank of stored frozen sera obtained from 14-20 weeks' gestation in conjunction with genetic amniocentesis for fetal karyotype, we randomly selected 313 euploid cases and 31 DS cases for evaluation. Using SAS Interactive Matrix Language, a generalized form of a multivariate Gaussian algorithm was created and utilized to generate likelihood ratios (LR) for DS. The product of this LR and the woman's age-risk of DS yielded a Summary Risk (SR) value (positive = Summary Risk ≥ 1:190). Available analytes included alphafetoprotein (AFP), unconjugated estriol (E_3), intact & free-beta human chorionic gonadatropin (IhCG, FβhCG), dimeric inhibin-A (IH-A) and cancer antigen 125 (CA-125). Based on the observed differences in mean analyte multiples of the medians between DS and euploid cases, we selected AFP, E_3, FβhCG, IH-A and CA-125 as having the best discriminant value, and included these for final evaluation in the pentavariate model.

RESULTS: The mean maternal age of our study population was 35 ± 5 yrs, and accounted for the generally high screen positive rates observed. The pentavariate model was superior to the analyte combination in most common usage (AFP-E_3-IhCG) using a receiver operating characteristic analysis ($p = .01$). At a Risk cut-off of 1:190 the pentavariate model had both a lower screen positive rate (19% vs. 28%) and a higher detection rate (97% vs. 85%).

CONCLUSIONS: Inclusion of five serum markers with good discriminate value in a pentavariate model results in superior performance of the MMST for DS.

299 **ACCEPTANCE OF AMNIOCENTESIS AFTER A POSITIVE TRIPLE MARKER SCREEN FOR DOWNS SYNDROME.** *J Weeks, N Cavil[x], T Hogue[x], CV Rao.[x]* Dept. of OB/GYN, Univ. of Louisville, Louisville, KY.

OBJECTIVE: The purpose of this retrospective study was to determine what clinical factors were associated with a patient's decision to accept or decline genetic amniocentesis after a positive maternal screen for Downs Syndrome.

METHODS: Patients who were referred to the obstetrical ultrasound units at the University of Louisville or the Alliant Women's Pavilion for evaluation of an abnormal triple marker screen from 1/93 to 5/94 were included. All patients were scanned and counseled by a Maternal-Fetal Medicine subspecialist. Additional counseling was provided by a geneticist except when patients declined the service or when a geneticist was not available. All clinical data was obtained by review of the triple marker lab reports and obstetrical ultrasound reports. Triple marker results were routinely reported along with a numerical risk for Downs (e.g. 1 in 128). The independent variables of interest were: patient age, parity, triple marker risk, ultrasound result (normal or abnormal), and whether the patient had additional counseling by a geneticist as opposed to counseling by the Maternal-Fetal staff only.

RESULTS: 331 patients were identified, 172 received genetic counseling (52%) and 139 accepted amniocentesis (42%). The average maternal age was 29 ± 7 years and the average risk for Downs was 1 in 108 ± 79. When a computer modeled stepwise logistic regression analysis was used to evaluate the influence of the 5 independent variables on the patient's decision to accept genetic amniocentesis, only one factor was clinically significant: counseling by a geneticist (see table).

Independent Variable	*Odds Ratio*	*p Value*
Genetic counseling	4.25	<0.0001
Age	1.07	0.003
Parity*	0.78	0.04

*Due to multiple comparisons, significance = 0.01

CONCLUSIONS: Genetic counseling was associated with greater acceptance of amniocentesis in patients who were referred for evaluation of an abnormal triple marker test. Prospective studies are needed to determine if the increase in patient acceptance is due to more effective patient reassurance, a better understanding of the value of amniocentesis or other factors unrelated to the patient's clinical situation.

300 **MATERNAL URINE SCREENING USING DRIED SPECIMEN TECHNOLOGY: COMPARISON OF FREE-BETA HCG AND BETA CORE FRAGMENT.** *T. Hallahan[1x], D. Krantz[1], B. Brambati[2], L. Tului[2], P. Buchanan[3], F. Orlandi[4], V. Klein[5], J. Larsen[6], J. Macri[1].* [1]NTD Laboratories, Inc. Huntington Station, NY, [2]First Institute OB/GYN, Univ. of Milan, Italy, [3]GeneCare Medical Genetics Center, Chapel Hill, NC, [4]Prenatal Diagnosis Service, Cervello Hospital, Palermo, Italy, [5]North Shore Univ. Hospital, Manhasset, NY, [6]George Washington Univ., Washington, DC.

OBJECTIVE: To compare the effectiveness of free-Beta hCG and Beta Core hCG in a dried urine Down Syndrome screening protocol.

STUDY DESIGN: We analyzed dried maternal urine specimens from 164 control, 9 Down syndrome affected and 4 trisomy 18 affected pregnancies between 8-25 weeks for free-Beta hCG and Beta Core hCG (UGF, Toagosei, Inc.). Creatinine was used to normalize values. Gestational age specific medians and Multiples of the Median (MoMs) were calculated for each analyte.

RESULTS: Free-Beta and Beta-core hCG values were closely correlated in controls and affected cases ($r = 0.61$ and 0.95, respectively).

	Control Percentiles					*DS Detection*	
Analyte	*10*	*50*	*90*	*Ctrl SD LOGe*	*DS MoM*	*5% FP*	*10% FP*
free-Beta	0.37	1.03	2.21	.697	2.42	22%	56%
beta-core	0.28	0.96	2.67	.879	2.40	33%	44%

In the four cases of Trisomy 18 the free-Beta hCG median MoM was 0.35 while that of Beta Core hCG was 0.51.

CONCLUSIONS: This study confirms an earlier report of Spencer et al. in which urinary free-Beta and beta-core showed similar elevations in DS cases. Urinary free-Beta MoMs in DS cases are similar to those found in serum, however, the wider distributions observed in urine may decrease screening efficiency. Beta core values in DS cases appear to be more similar to free-Beta than seen in other small series. Additional evaluation of assay specificities are required to determine the cause of observed discrepancies among studies.