

**Fetal Defect Marker Proficiency Test Mailout from May 8, 2007
June, 2007**

Dear Laboratory Director,

Below you will find a summary and critique of the Proficiency Testing mail-out from May 8, 2007 for Fetal Defect Markers, including AFP, uE3, hCG, and dimeric inhibin-A. Your laboratory's results and grades are printed on a separate sheet; also included are the grades from the previous two PT events. Please review and sign your evaluation. Retain the signed packet in your files. You will need it for your next laboratory survey to demonstrate participation in the NYSPT program.

Second Trimester Maternal Serum: Summary of Sample Results

Samples *N = 30	Sample #	MS 206	MS 207	MS 208	MS 209	MS 210
	Gestational Age (weeks)	16.0	17.0	18.0	15.0	19.0
Maternal Race	Ethnic Group	Black	White	Hispanic	Asian	White
Maternal Weight	Pounds (lbs)	195	135	140	115	125
Maternal Age	Years	25	28	20	23	32
Alpha-Fetoprotein (AFP)	Mean ng/mL	95.09 ± 7.50	88.14 ± 6.83	46.96 ± 3.71	31.85 ± 2.60	25.19 ± 2.03
	MoM	3.03 ± 0.31	2.13 ± 0.13	1.02 ± 0.08	0.93 ± 0.07	0.44 ± 0.03
Unconjugated Estriol (uE3)	Mean ng/mL	1.01 ± 0.33	1.33 ± 0.46	1.79 ± 0.65	0.83 ± 0.23	0.93 ± 0.29
	MoM	0.81 ± 0.21	0.75 ± 0.19	0.80 ± 0.16	0.73 ± 0.21	0.34 ± 0.10
human Chorionic Gonadotrophin (hCG)	Mean IU/mL	35.45 ± 2.80	31.27 ± 2.65	26.63 ± 2.46	45.71 ± 3.98	55.75 ± 5.83
	MoM	1.26 ± 0.14	1.20 ± 0.14	1.21 ± 0.18	0.99 ± 0.12	2.64 ± 0.31
Dimeric Inhibin-A (DIA)	Mean pg/mL	137.2 ± 12.86	144.2 ± 14.51	147.2 ± 14.51	142.4 ± 13.38	437.1 ± 40.56
	MoM	0.89 ± 0.10	0.81 ± 0.10	0.84 ± 0.10	0.66 ± 0.11	2.25 ± 0.33
Neural Tube Screen (Positive, Negative)	Pos (+) or Neg. (-)	Pos. (93%)	Neg. (B) (62%)	Neg. (100%)	Neg. (100%)	Neg. (100%)
	Further Action R,U,A	R = 46% U = 68% A = 40%	R = 14% U = 14% A = 0	NFA	NFA	NFA
	NTD Risk 1:	194	514	8,000	9,000	7,900
Trisomy-21 Screen (Positive, Negative)	Pos (+); Neg.(-)	Neg. (100%)	Neg. (100%)	Neg. (100%)	Neg. (100%)	Pos. (100%)
	Recommended Action **	NFA	NFA	NFA	NFA	U = 74% A = 79%
	Risk Est. 1:	10,000	10,000	10,000	10,000	28
2. <u>Quad Test</u>	Pos (+); Neg. (-).	Neg. (100%)	Neg. (100%)	Neg. (100%)	Neg. (100%)	Pos. (100%)
	Recommended Action **	NFA	NFA	NFA	NFA	U = 76% A = 68%
	Risk Est. 1:	20,000	20,000	12,000	16,000	7
Trisomy-18 Screen (Positive, Negative)	Pos (+)/Neg. (-)	Neg. (-)	Neg. (-)	Neg. (-)	Neg. (-)	Neg. (-)
	Risk Est. 1:	10,000	7,500	10,000	6,100	601

*N=total numbers may vary since some labs do not test all analytes. The values represent the All-Lab consensus based on the arithmetic mean ± SD; (B) = borderline positive or negative, risk reflects central tendency (Modal number for Down positive/borderline screen). NFA = no further action; FA = further action; R = repeat; U = ultrasound, and A = amniocentesis.
**This percentage is normalized to labs requesting further action. † Insulin Dependent Diabetic pregnancy.

Notice of Gravida/Parity Clarification for Present and Future Mailouts:

This notice regards the demographic data provided for the mock patients in the FEDM program. For the sake of uniformity, it will be understood that gravida indicates a pregnant woman and parity is the state of having given birth to an infant or infants. Thus, a gravida = n, indicates number (n) of times pregnant including the present one; a gravida = 2 indicates that the woman was pregnant once before in addition to her present pregnancy. Parity = 1 indicates the patient already has one child; also, multiple birth is considered as a single parity.

Example: A woman of gravida = 3, parity = 2 indicates that the pregnant woman has been pregnant twice before, and has two children.

AMNIOTIC FLUID AFP (NTD-analysis):

N=30; All-Lab Consensus Values

<u>Sample</u>	<u>Values</u>	<u>Summary Comments:</u>
AF 206 Wk 18.0	AFP= 11.7 ± 1.8 µg/ml MOM= 1.20 ± 0.12	This sample was targeted for a screen negative AF AFP value in the upper routine gestational age range. All labs reported this specimen as a screen negative value. The AF206 specimen was not paired with an MS specimen.
AF 207 Wk 17.0	AFP= 27.4 ± 4.0 µg/ml MOM= 2.34 ± 0.30	This sample was targeted for a borderline elevated AF AFP value in the routine gestational age group. Most labs (93%) called it an elevated specimen for NTD depending on the individual lab MoM cutoff values. This AF AFP sample was matched to MS207 (see critique) which screened borderline negative for NTD.
AF 208 Wk 18.0	AFP= 10.5 ± 1.2 µg/ml MOM= 1.09 ± 0.11	This sample was targeted for a screen negative AF AFP value in the upper routine gestational age screening range. All labs categorized this as a screen negative specimen. AF208 was matched to MS208 which also screened negative for NTD.
AF 209 Wk 19.0	AFP= 4.9 ± 0.6 µg/ml MOM= 0.62 ± 0.07	This sample was targeted as a screen negative AF AFP value in the upper gestational screening range. All labs categorized this as a negative AF AFP specimen; it had no maternal serum counterpart.
AF 210 Wk 20.0	AFP= 9.9 ± 1.3 µg/ml MOM= 1.53 ± 0.18	This sample was targeted for a screen negative AF AFP value in the upper routine gestational age range. All labs classified this as a negative (non-elevated) specimen. This AF AFP sample was not matched to an MS sample.

Fetal Defect Proficiency Test Mailout 5/8/07 Critique of Maternal Serum and Amniotic Fluid Values:

The all-lab results of the targeted values for the NTD and the Trisomy Screen achieved the expectations of our projected target values, risks, and outcomes. As displayed in the above tables, maternal sera MS206 and MS207 were targeted as a positive and a borderline elevated for NTD, respectively (Fig. 1 and 3). Specimen MS207 was from a patient with a prior pregnancy loss and presently screened borderline negative for NTD. For specimen MS206, which screened NTD positive, the all lab recommended actions (see below) were as expected; correspondingly, the NTD screen for MS206 resulted in a 1:194 risk for open neural tube defects (ONTD) and the positive screen achieved a 93% all-lab consensus. The recommended action for the MS206 specimen was the following: sample repeat, 46%; ultrasound; 68%; and amniocentesis, 40%. It is germane to this specimen that the all-lab median MSAFP cutoff value for the Afro-American population (in our participating labs) is 2.5 MOM. Sample MS207, a borderline NTD screen negative result, was obtained from a Caucasian woman with a prior history of personal pregnancy loss; her AF specimen screen also resulted in a borderline elevated screen AFP value (see Figure-2). The borderline negative screen for sample MS207, in the face of an MS-MOM of 2.1, did not approach the cutoff values held by participating laboratories, and only 38% of the labs recommended further action. In view of the MS207 screen results however, her borderline elevated amniotic fluid AFP specimen (MOM = 2.34) would suggest the need for further Ache and fetal hemoglobin analysis. Specimens

MS208, MS209, and MS210 were all targeted and achieved negative screens for NTD, with all labs recommending no further action. Of these samples, MS210 produced a positive screen for Trisomy-21 which is discussed below. Finally, the MS209 specimen was obtained from a woman of Asian descent and indicated both ethnic and body weight adjustments (lower truncation) in her risk assessment calculations.

Specimen MS207, with a matched AF AFP, proved to be an interesting case in that the MSAFP specimen was borderline screen negative and her paired AF AFP specimen screened borderline elevated (MOM = 2.34) depending on differential lab cutoff values (Fig. 1 & 2). This mock patient had a personal history of pregnancy loss and a family history of adverse outcomes; thus, a paired maternal serum sample was obtained at time of amniocentesis. Her MSAFP MOM of 2.13, although borderline MS screen negative, was accompanied by an amniocentesis AF AFP outcome which indeed proved to be NTD borderline elevated. A high definition Stage-II ultrasound together with a Ache analysis later confirmed the presence of a small open NTD lesion in the spinal cord from the fetus of this mock patient. An all-lab NTD risk assessment for MS207 was calculated as 1 in 514 for maternal serum alone.

The maternal serum screen for MS208 (Gravida 2.0, parity 1.0) produced definitive negative screens for both NTD MSAFP (MOM = 1.3) and trisomy-21 (MSAFP MOM = 1.02). Moreover, the sample was accompanied by an amniotic fluid (AF) specimen which also proved to be NTD screen negative. The AF specimen had been obtained at time of amniocentesis due to a family history of neural tube defects in sibling related pregnancies. The amniocentesis was performed as a failsafe procedure due to the prior family history and to reduce anxiety in the patient. The maternal serum was procured immediately prior to the amniocentesis and the procedure produced no indication of a fetal bleed.

Regarding the trisomy screen, the MS210 specimen (gravida = 1, parity = 0; maternal age = 32) was intended to produce a positive Trisomy-21 (T21) screen with both the triple and quad testing platforms, which indeed was the case. The labs reporting either triple or quad testing concluded that sample MS210 was T21 screen positive (100% all lab consensus). Further action recommended for the T21 screen was determined as 74% ultrasound (US) and 79% amniocentesis (AM) for labs using the triple screen, and 76% US and 68% AM for labs employing the quad screen. Further recommended action on MS210 reflected the severity of the risk ratio assessment of 1:28 risk from the triple test versus 1:7 risk from the quad test, regardless of the software program employed. Note from the point distribution graphs comparing the triple with the quad test (Figs. 5 and 6) that the MS210 point cluster in the quad assay was just slightly lower than the MS210 cluster in the triple test. Again, the quad test clearly signaled a slightly higher risk for Down syndrome while the triple test also yielded a significant risk; overall both screens signaled a very high risk for Down Syndrome. The quad and triple risks of DS were greater than that expected from the maternal age alone (1 in 510).

The performances of the various kits for maternal serum analytes (AFP, uE3, hCG) are presented in a bar graph format (Figures 7-9) for each of the five MS samples. As shown in the MS-AFP graph, AFP mass measurements among the individual kits largely agreed, although Bayer-Centaur was somewhat higher, while DPC Immulite and Beckman Unicel were marginally lower for some samples. For uE3, the all lab median was higher than 1.0 (see tables) due to the labs employing DPC Immulite and DPC Immulite 2000 which yielded values nearly two times higher than the median. In contrast, Diagnostic Systems Lab RIA/EIA results were at the mean level while Beckman Access measured uE3 values nearly 20% lower than the median. These results continue to demonstrate some inherent differences as to how these assays recognize the uE3 in our mock sample preparations. Regarding the hCG kits, laboratories employing Abbott AxSYM values were not displayed due to kit recall and technical difficulties, while Bayer-Centaur, Immulite, and Beckman Access all yielded equivalent means (1.0) hCG values. In order to enhance uniformity among the various kits employed to measure hCG, we incorporate an intact (total) hCG recombinant analyte into our PT specimens. Labs lacking peer group companions and in-house assays will continue to be deemed non-gradable (NG) for hCG as well as other analyte groups as the situation dictates.

The bar graph in Figure 10 is provided to display kit performance among the amniotic fluid (AF-AFP) test samples. As shown in the amniotic fluid bar graph, overall kit performance approached that observed with the maternal serum samples. While Bayer-Centaur, and to a lesser extent Abbott-AxSYM kits were higher, Beckman Access and DPC Immulite were slightly lower than the all-lab mean as seen in previous mailouts. It was of interest that specimen AF207 produced a borderline negative NTD screen (MOM = 2.34) in the face of a MSAFP screen MoM value of 2.1 (see above discussion and Figures 1&2). Note that the point distribution in the AF AFP-207 MOM values (Figure 2) produced a range of values extending from 2.00 to nearly 2.7 MOM, while the MSAFP values extended from 1.75 to 2.3 MoM. In general, there exists a slight trend among kits suggesting that the higher AF AFP mass results correlated with the higher AF AFP MOMs. Finally, please be advised that these

specimens are derived from actual AF samples, and therefore these results are directly relevant to patient screening.

For informational purposes, it was deemed of interest to post the software usage by our participating laboratories. The alpha and Benetech software packages are each used by 22 and 17%, of the labs respectively; RMA software is employed by 34%; while in-house software comprised 19%, and 6% of labs use programs classified as “other” which are proprietary software packages.

First Trimester Screen:

A first trimester maternal serum mock sample was included in the present mailout as an investigational probe for future Down syndrome First Trimester mailouts. The probe was mailed out in order to survey New York State licensed laboratory clientele concerning lab participation and assay capabilities in first trimester screening for DS. The results will not be graded and the survey results are intended to serve as an information gathering event in anticipation of possible future mail-out implementation. Laboratories that are validation-approved and presently performing first trimester Down screening are required to test and report screen results from the present mailout. Those laboratories not presently offering the test, or not planning to implement the test, can request that no further samples be sent (see result answer sheet). The present sample FT206 (FT = first trimester) information provided to lab participants included maternal age, nuchal translucency (NT), crown-rump length (CRL) measurements, last menstrual period (LMR), and draw date. Race and body weight will be included in future mailouts. The gestational age all-Lab mean was 11.8 weeks. Measurements from FT-screening participating laboratories resulted in the All-Lab total hCG MOM measurement of 1.63 based on two methods, namely, Beckman (BCU or BCX/BC1) and DPC/Siemens (DPD or DPB/DP5); while the All-Lab PAPP-A MOM assessments were 3.21 (see Figs 11 and 12). The all-lab (N = 12) trisomy-21 screen consensus was negative. The all-lab FT trisomy-21 risk assessment was 1 in 8,000, while the Down’s risk due to maternal age alone was 1 in 450.

As observed in the First Trimester table (Section – B) table above, the all lab measurement of total hCG achieved an arithmetic mean of 121.93 IU/mL \pm 17.93. However, the hCG percent CV resulted in a value of 14.79 demonstrating a high variance among the participating labs. Second trimester hCG CVs usually ranged from 7 to 10%. In comparison, the all-Lab mean for PAPP-A was 4.51 \pm 2.48 mIU/mL. (Figures 11 & 12). The high standard deviation demonstrated by the PAPP-A measurement consequently yielded an all-Lab % CV of 55.1% due to the differential values of the Beckman/Diagnostic Systems Labs kit (CV = 16.8%) versus the DPC/Siemens Immullite kit (CV = 7.8%) (see Figure 12 Medians). Despite the disparate variances in which the PAPP-A DPC median was quite high (1.4) compared to Diagnostic systems (0.6), all labs agreed that the FT sample was screen negative (See Figure 13 point distribution). The lab risk cut-off levels (W = 12) were found to range from 200 to 270. Since PAPP-A measurements for first trimester Down Syndrome are associated with low MOM values, high MOMs would be consistent with a screen negative outcome.

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New References (Suggested reading):

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Abstracts

A). Screening Abstract “Pick-of-the-Month”:

(1) Title: Predicting the result of additional second-trimester markers from a woman’s first-trimester marker profile: a new concept in Down syndrome screening.

Source: Prenatal Diagnosis. 25 (12): 1102-1106, 2005.

Authors: Maymon R, Cuckle H, Jones, R, Reish O, Sharony R, Herman A.

Abstract: **Objective:** To describe a method for deciding whether an individual’s first-trimester Down syndrome screening test result justifies further testing in the second trimester. **Methods:** Statistical modeling was used to estimate the distribution of second-trimester marker profiles for a given first-trimester profile and hence the probability of a final positive result, using a 1 in 250 term cut-off. A multi-variate log Gaussian model was used with published parameters. Markers were maternal serum pregnancy-associated plasma protein-A and free beta-human chorionic gonadotrophin (hCG) at 10 weeks, nuchal translucency at 11 weeks, and second-trimester maternal serum alpha-fetoprotein, total hCG, unconjugated estriol and inhibin-A. To illustrate the method, the model was applied to a published series of 24 Down syndrome and 367 unaffected pregnancies. **Results:** Modelling predicts that for 63% Down syndrome and 0.4% unaffected pregnancies having first-trimester tests, there is a 50% or more probability of a final positive result. A step-wise sequential screening policy based on immediate prenatal diagnosis for those with high probability and second-trimester testing for the remainder would have a 90% detection rate and 1.7% false-positive rate. Modelling also predicts 8.0% Down syndrome and 89% unaffected pregnancies with probabilities below 3%. A contingent screening policy restricting second-trimester testing to those with 3-49% probabilities would have an 88% detection rate and 1.4% false-positive rate. **Conclusion:** Predicting the probability of a positive final result from the first-trimester marker profile has potential utility, either as a decision aide for individual women or as a formal part of screening policy in selecting a subset of women for second-trimester testing.

(2) Title: Screening for aneuploidy in first and second trimesters: is there an optimal paradigm?

Source: Current Opinion in Obstetrics & Gynecology. 19(2): 176-182, 2007.

Authors: Breathnach FM, Malone FD.

Abstract: Purpose of review. This review serves to explore the recent literature regarding aneuploidy screening in both first and second trimesters. We aim to construct a comparative analysis of a range of proposed strategies for screening for trisomy 21.

Recent findings First trimester combined screening (sonographic nuchal translucency combined with serum markers pregnancy-associated plasma protein A and the free beta subunit of human chorionic gonadotrophin) has superseded second trimester serum screening (alpha-fetoprotein, total human chorionic gonadotrophin, unconjugated estriol with or without inhibin-A) as a screening paradigm for the detection of trisomy 21. This move is attributed to the recognition of superior detection rates, lower false-positive rates and earlier results associated with the former strategy. Septated cystic hygroma has been recognized as a distinct entity which confers a high risk of aneuploidy and structural malformations, further advances in screening performance are achievable by combining the results of first and second-trimester screens in a sequential manner, with much interest generated by programs that only include second-trimester testing contingent upon first-trimester results.

B). Case History Screening “pick-of-the-month”:

(1) Title: Beckwith-Wiedemann syndrome presenting with an elevated triple screen in the second trimester of pregnancy.

Source: Fetal Diagnosis & Therapy. 22: 18-22, 2007.

Authors: Aagaard-Tillery KM, Buchbinder A, Boente MP, Ramin KD.

Abstract: **Background:** Beckwith-Wiedemann syndrome (BWS) is a distinct clinical syndrome with unique features, is generally diagnosed postnally. Case: A 26-year-old patient, gravida 4, para 3-0-0-3, was noted to have an abnormal maternal serum screen. Amniocentesis with imaging studies was remarkable for observing a two-vessel umbilical cord and prominent maternal ovaries. The patient developed HELLP syndrome at 28 weeks and delivered a viable female infant with distinct clinical features. The diagnosis of TWS was confirmed by hypermethylation of the H19 gene on chromosome 11p15.5. **Conclusion:** This case describes a novel presentation of BWS and underscores the diagnostic potential of routine prenatal screens.

(2) Title: Prenatal detection of deletion 6q13q15 in a complex karyotype. [Review] [10 refs]

Source: Prenatal Diagnosis. 25(12): 1084-1087, 2005.

Authors: Yu M, Obringer AC, Fowler MH, Hummel M, Wenger SL.

Abstract: **Objectives:** Prenatal diagnosis of a pregnancy with elevated maternal serum alpha-fetoprotein identified a karyotype with a complex chromosomal rearrangement, a Robertsonian translocation and a 6q deletion involving bands q13q15. Sonography identified mild IUGR, polyhydramnios and micrognathia. The infant presented with multiple congenital anomalies, primarily limited to the head and neck, including hypertelorism, broad nose, micrognathia, cleft palate, microglossia and low-set ears with microtia. **Methods:** Amniocytes of the fetus and blood of the patient and her parents were analyzed by cytogenetics and fluorescence in situ hybridization. **Results:** The karyotype on the fetus was 45,XX,t(3;21;20) (p12;q11.2;p11.2), del(6)(q13q15), der(13;14) (q10;q10)mat. **Conclusion:** The 13;14 Robertsonian translocation was inherited from the mother and the three-way translocation appeared to be balanced. The patient has facial dysmorphism similar to that which has been described in 6 previously reported cases with the same deletion involving 6q13q15. There was no recognizable abnormality of limbs or digits, and the autopsy did not identify defects involving the internal organs. [References:10].

C). **News of Notes: Abstract of New Markers and/or New Testing Agents:**

(1) Title: Routine assessment of amniotic fluid alpha-fetoprotein in early second-trimester amniocentesis is no longer justified.

Source: Acta Obstetrica et Gynecologica Scandinavica 86(2): 167-171, 2007.

Authors: Widlund KF, Gottvall T.

Abstract: **Background:** Open fetal neural tube defects are often followed by an increase in alpha-fetoprotein concentration in amniotic fluid. For over 25 years there has been a routine to measure amniotic fluid alpha-fetoprotein in conjunction with early genetic amniocentesis. The efficacy of such a screening test in a low-risk population has been questioned but never evaluated in a Swedish population. **Methods:** Data were reviewed retrospectively from all consecutive early second-trimester genetic amniocenteses from two hospitals during the years 1993-2003. Indications for the genetic amniocenteses were maternal age > or = 35 years, maternal anxiety or a history of fetal aneuploidy. A questionnaire was sent to all obstetric clinics in Sweden regarding current common policy and experience of routine amniotic fluid alpha-fetoprotein measurements, in the detection of open fetal neural tube defects. **Results:** A total of 1,813 samples were included. In eight cases (0.4%) the amniotic fluid alpha-fetoprotein concentrations were > or = 3 multiples of median, but five of them were false positive (63%). Out of the three true positive cases, one had clinical relevance. In the other two cases the detection of open fetal neural tube defects was of subordinate importance. In Sweden, during 2004, 91% of the obstetric clinics performed routine assessment of amniotic fluid alpha-fetoprotein at second-trimester genetic amniocenteses, but only 9% regarded the analysis useful in clinical practice. **Conclusions:** According to our results, routine measurement of amniotic fluid alpha-fetoprotein in early second-trimester genetic amniocentesis, to rule out a risk of open fetal neural tube defects, does not seem justified. The clinical usefulness seems to be limited.

(2) Title: Fetal anomaly scan potentially will replace routine AFAFP assays for the detection of neural tube defects.

Source: Prenatal Diagnosis 27(1): 29-33, 2007.

Authors: Kooper AJ, de Bruijn D, van Ravenwaaij-Arts CM, Faas BH, Creemers JW, Thomas CM, Smits AP.

Abstract: **Objectives:** Introduction of the second-trimester fetal anomaly scan and the decision to offer this scan to every woman in the 18th-22nd week of pregnancy necessitates a re-evaluation of the diagnostic value of the measurement of alpha-fetoprotein (AFP) concentrations in the amniotic fluid (AF) for the detection of neural tube defects (NTDS). **Methods:** In this study of 6501 women who underwent amniocentesis, amniotic fluid AFP (AFAFP) concentrations were measured. The women were divided into three categories: group I, without any increased risk of fetal NTD (N = 6188); group II, with an increased risk of fetal NTD (N = 258); and group III, with a clinically diagnosed fetal NTD with known AFAFP concentrations (N = 55). **Results:** In 27 women of group I (0.4%), the MoM (multiple of the median) level was > 2.5 times the median AFP concentration for the corresponding gestational age, and in two fetuses this was related to NTD. In two pregnancies of group II (0.8%) samples had an increased AFAFP. **Conclusion:** In the near future, it is likely that imaging will replace AFAFP assays for the detection of fetal NTDs because high quality ultrasound imaging will detect NTDs accurately.

D). **Review Article “Pick of the Month”**

(1) Title: Tumor markers in biological fluids associated with pregnancy [Review]

Source: Critical Reviews in Clinical Laboratory Sciences. 44(2): 151-178, 2007.

Authors: Sarandakou A, Protonotariou E, Rizos D.

Abstract: Proteins that are expressed by both malignant and healthy fetal tissues are recognized as oncofetal. These antigens are associated with cell proliferation and differentiation and are produced in high concentrations in pregnancy and malignancy. Their biological role in malignancy is the suppression of the host's immune system, while in pregnancy they affect the maternal immune response, generating maternal tolerance toward the embryo. This review describes the levels of alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), carcinoembryonic antigen (CEA), cancer antigen 125 (CA 125), squamous cell carcinoma antigen (SCC), cancer antigen 15-3 (CA 15-3), mucin-like carcinoma-associated antigen (MCA), tissue polypeptide-specific antigen (TPS), carbohydrate antigen 19-9 (CA 19-9), and prostate-specific antigen (PSA) in maternal serum (MS), umbilical cord serum (UC), and amniotic fluid (AF) and outlines their roles in the assessment of pregnancy and malignancy. All antigens studied, except CA 15-3, are oncofetal. The presence of considerable concentrations of AFP, hCG, CEA, CA125, SCC, MCA, TPS, CA 19-9, and PSA and AF during pregnancy may be attributed to their involvement in biological functions associated with fetal development, differentiation, and maturation. MS CEA, CA 15-3, and CA 19-9, in contrast to all the others, are not influenced significantly by pregnancy and thus remain reliable tumor markers in monitoring malignancy in pregnant patients [References: 163].

(2) Title: Mosaic trisomy 16 in a fetus: the complex relationship between phenotype and genetic mechanisms [Review]

Source: Prenatal Diagnosis. 26(12): 1179-1182, 2006.

Authors: Moradkhani K, Puechberty J, Blanchet P, Coubes C, Lallaoui H, Lewin P, Lefort G, Sarda P.

Abstract: **Objectives:** This study was undertaken to discuss the workup of trisomy 16 pregnancies. **Study Design:** This case study reports the prenatal detection and postnatal confirmation of mosaic trisomy 16, associated with uniparental disomy (UPD) 16, in a 34-year-old woman who showed elevated maternal serum alpha-fetoprotein and beta-HCG at a gestational age (GA) of

15.5 weeks. **Results:** Amniotic fluid (AF) karyotyping at different Gas revealed various levels of trisomy 16 mosaicism (0 to level III). UPD studies at 21 weeks of gestation revealed maternal heterodisomy 16. Serial fetal ultrasonography showed fetal abnormalities: intrauterine growth restriction (IUGR), dilated digestive tract, and gallbladder agenesis. Postmortem examination confirmed the prenatal findings and revealed additional anomalies, such as hypoplastic cerebellum with abnormal gyration of the vermis. **Conclusions:** Workup following prenatal detection of trisomy 16 mosaicism in chorionic villi must include AF karyotyping and serial ultrasound examination of the fetus in order to approach postnatal developmental prognosis.