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Thyroid Congress

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## POSTER PRESENTATION CERTIFICATE

We hereby certify that:

**Timothy Bilash**

has presented the poster N° **P-0546**

Title :

**THYROID STIMULATING HORMONE (TSH) AND FREE THYROXINE LEVELS (FT4) IN  
PREGNANT FEMALES >25 WEEKS GESTATION AND NON-PREGNANT FEMALES WHO HAVE  
CLINICAL PROBLEMS AND HYPOTHYROID SYMPTOMS: EVIDENCE SUPPORTING POOR  
CORRELATION BETWEEN TSH AND FT4**

on the occasion of the :

14<sup>th</sup> International Thyroid Congress  
which has been held at the  
Palais des Congrès, Paris, France  
September 11th to 16th, 2010

These are slides from the 2010 Poster with additional clarification

**25. Clinical thyroidology – Case reports**

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**Preferred Presentation Method: Poster Presentation**

**ITC2010-561**

**Thyroid Stimulating Hormone (TSH) and Free Thyroxine Levels (FT4)**

**In Pregnant Females >20 weeks gestation and Non-Pregnant Females**

**who have Clinical Problems and Hypothyroid Symptoms:**

**Evidence Supporting Poor Correlation between TSH and FT4.**

## Abstract:

### METHOD:

**14 Pregnant** Females at greater than 20 weeks gestation and **14 Non-Pregnant** Female patients in an upstate New York rural community Obstetrics and Gynecology office presented with a variety of clinical problems in Pregnancy (**preterm labor, obesity, gestational diabetes, supraventricular tachycardia, pyelonephritis**) and Non-Pregnancy [**oligomenorrhea, infertility, bleeding, uterine myoma, atrial arrhythmia, ovarian cyst**] and were **screened at the time of presentation** with Serum Thyroid Stimulating Hormone and Free Thyroxine Assays (**AxSym, Abbott** Laboratories, Abbott Park, IL). Some patients were treated with Levo-Thyroxine. Test results and clinical observations were tabulated.

**RESULTS:** In these **problem patients:**

For the **Pregnant** patients,

**Thyroid Stimulating Hormone** [0.51-5.08, **Mean=1.94**, SD=1.32 MIU/L] and

**Free Thyroxine** [0.57-0.92, **Mean=0.69**, SD=0.11 ng/dl] were both

found to be uncorrelated with Gestational Age at greater than 20 weeks gestation.

For the **Non-Pregnant** patients,

**Thyroid Stimulating Hormone** range was 0.96-7.35 [**Mean=3.71**, SD=1.95] and

**Free Thyroxine** range was 0.51-0.99 [**Mean=0.81**, SD=0.15].

For the **Pregnant** patients compared to **Non-Pregnant** ones,

**Thyroid Stimulating Hormone** averaged **-1.77 MIU/L lower** (SE=0.10) and

**Free Thyroxine** was **-0.12 ng/dl lower** (SE=0.01).

**Free Thyroxine** level also appeared to be **independent of Thyroid Stimulating Hormone** level in both the **Pregnant** patients greater than 20 weeks gestation and **Non-Pregnant** patients.

## DISCUSSION:

The often described inverse log-linear relationship between serum FT4 and TSH (FT4 =  $-\log TSH$  at TSH setpoint) focuses on regulation about the TSH setpoint, describing the control mechanism for TSH when FT4 moves away from equilibrium. Little is understood about the control mechanism in Pregnancy which may alter the TSH setpoint itself. These findings indicate a possible alteration in the Pituitary setpoint rather than feedback to or suppression of the Thyroid Gland itself, particularly because neither FT4 nor TSH was correlated with Gestational Age at greater than 20 weeks gestation.

Some patients (both Pregnant and Non-Pregnant) were treated with low doses of Levo-Thyroxine and showed improvement of their immediate clinical problems.

### Additional Clinical Observations:

- 1) T4, T3, T2 and HCG all suppress TSH.
- 2) Pregnant patients with a higher TSH may actually drop their FreeT4 if dosing is inadequate by suppression of TSH to more normal values.

NAME	AGE	DX	DATE	PREG wks	TSH	FT4	FT4calc	FT4-calc	FT3	TT4	T3	UPFSH	LH	TT4/FT4	OTHER COMMENTS	TSH's	FT4's	T3U's	TT4
<b>PREGNANT/(WITH PROBLEMS)</b>																			
F-1	40	4wk SAB early no site, G2P1	09/12/02	4	1.32	0.93	0.68	0.25							Low FSH,LH;Rhneg,bHCG=8(9/10),=2(9/11)				
F-2	35	6wk SAB,BTL failure	09/13/02	5	3.22	0.83	0.79	0.04		5.7				6.87	HCG=43, bleeding				
F-3	29	8wk SAB/D&C,+ACA11,-ANA	08/24/02	6	6.84	1.05	1.01	0.04							sxs, increase to 75 (ACA=11 on 9/27)	4.59	0.99		
F-4	28	20wk	09/09/02	8	5.22	1.01	0.91	0.10							stopped LT(0.88)wks4-7,BlgtOvum				
T-1	26	27wk pyelonephritis,+UGBS,++fatigue	01/24/02	20	3.61	0.88	0.82	0.06							-				
T-2	21	29wk pyelo,eatdis,ptl	07/02/02	40											on LT50	1.5			
T-3	29	DM	09/24/02	27	1.56	0.60	0.69	-0.09							start LT75,^HC/AC,improved9/26				
T-4	32	hthsxs,UTI,breech,GDM,urethdivert [EGA?]	08/29/02	29	0.51	0.76	0.63	0.13	2.8	11.8				15.53	start LT50,recurrent UTI,mg1.1,hiTbG,loUII2	0.79	0.8		
T-5	29	PTL,dehydration	09/12/02	31											hydro,dil fetal renal				
T-6	29	34wk SVT,PTL,UTI,IUGR	08/16/02	30											CR=1.1,CrCl=106				
T-7	32	1CS FTP,41weeks,10#4,funisitis,mg=1.2	08/30/02	32	1.26	0.69	0.68	0.01							ST50				
T-8	35	35wk obese,fatigue,UTI,PTL,vagblid,330#	09/12/02	33											on ST50,^LT75,improved,Cr1.2,Mg1.0	1.31	0.58		14
T-9	32	35wk fetal demise,adrenal hypoplasia	08/14/02	32	1.90	0.58	0.71	-0.13							start 50 9/4,ABneg,fet wtgain,prevCS				
T-10	27	37wk MObesity,++c/o's	09/19/02	36											on LT50,improved	0.61	0.69		
T-11	21	PPD1,HTN,TOB2PPD	09/27/02	33	0.70	0.70	0.64	0.06							mg1.5				
T-12	22	1CS FTP,41weeks,10#4,funisitis,mg=1.2	08/20/02	34	1.52	0.57	0.69	-0.12		9.0				15.79	SVT50 to NSR				
			08/23/02	34											SVT recurred off LT4 (8/22)	1.63	0.72		11
			08/25/02	34											restart LT4 50				
			09/10/02	36											start LT4 75,fetus70%EFW,Cr1.2,CrCl232				
			09/12/02	36											on LT75,emesis,glu contrl	1.31	0.58		
			08/29/02	34	1.37	0.87	0.68	0.19							start LT50				
			09/28/02	36											Cr=1.1				
			10/02/02	35	5.08	0.63	0.90	-0.27		11.7					ST 75,staph,SVDx6,mg1.4				
			09/23/02	35	1.90	0.75	0.71	0.04							thrmbphl/cellulitis,hx depr,thyrsx,hx Hth				
			09/24/02	37	0.97	0.58	0.66	-0.08							SocEmotProbs,hx skin infects/ml stne/?PE				
			09/29/02	40	2.10	0.76	0.73	0.03	3.4						marginert,URI,neg thyrab,remoteHepC,mg1.5				
			09/24/02	40	2.16	0.60	0.73	-0.13							Alb1.8,hxBV				
			10/06/02	41	4.24	0.92	0.85	0.07							bradcard pp,hx Hthyr?,wtloss on depo,905gmsPL				

	TSH/FT4 Ratio	TSH	FT4	FT4calc	FT4-calc	TT4	TSH's	FT4's	T3U's	TT4
<b>PREGNANCY AVERAGE (WITH PROBLEMS)</b>	3.3	2.53	0.76	0.75	0.01	9.6				
<b>PREG AVG (for TSH&lt;2)</b>	1.9	1.30	0.70	0.68	0.02	10.4				
<b>PREG AVG (for TSH&gt;2)</b>	4.9	4.06	0.84	0.84	-0.01	8.7				
<b>TSH (TSH&lt;2 minus TSH&gt;2) Differences =</b>	-3.0	-2.76	-0.13	-0.17	0.03	1.7				
<b>PREG AVG (for &lt;20wks)</b>	4.3	4.04	0.94	0.84	0.10	5.7				
<b>PREG AVG (for &gt;20wks)</b>	2.8	1.94	0.69	0.72	-0.02	10.8				
<b>WKS (&lt;20wks minus &gt;20wks) Differences =</b>	1.5	2.10	0.25	0.13	0.12	-5.1				
<b>Preg Avg &gt;20wks/TSH &lt;2</b>	1.9	1.30	0.68	0.68	0.00					
<b>Preg Avg &gt;20wks/TSH &gt;2</b>	4.7	3.40	0.73	0.80	-0.08					
<b>TSH (TSH&lt;2 minus TSH&gt;2) Differences for WKS&gt;20wks</b>	-2.8	-2.10	-0.05	0.13	0.08					

for pregnant sick patients average FT4 is low, TSH hi

evidence for inadequate TSH, fails to augment FT4 average FT4 calc is predicted from TSH (inadequate TSH)

TBG higher >20weeks

expected TSH lower <20 weeks

TSH, FT4 are higher <20 weeks (T4 is lower)

TSH, FT4 decrease/ T4 increases with GA

TABLE 1 PREGNANT PROBLEMS PATIENTS

NON-PREGNANT/(WITH PROBLEMS)					TSH	FT4	FT4-AVG	FT3	TT4	T3 UPFSH LH	OTHER COMMENTS	TSH's	FT4's	T3U's	TT4
NAME	AGE	DX	DATE		.49-4.67	.71-1.85	delta	2.3-4.2	4.5-12.0	.6-1.27 0-20 0-20					
NP-1	21	Infert,anov	5/28/02		6.36	0.89	0.08			6.4 15	subclin,insulin=18(6-27)				
	-	-	7/24/02								on LT4 50	1.62			
	-	-	8/22/02								offT4(7/30-8/4),restart 8/5,start clomid	1.93	0.89		
NP-2	22	hx SAB,fatigue,anov/bicorut/anemia/SVD	9/11/02		0.96	0.78	-0.03			7 6.8	irreg menses,recurr ov cysts				
NP-3	26	IrregMenses	10/2/02		1.92	0.87	0.06			3 5.9	anovulation				
NP-4	43	hthsxs,loBMD,permnpsx,BV,scarpain	9/24/02		1.93	0.66	-0.15			4.2 3.4	Fibr/TAH,BV,constp,0.05/premphase(10/5)				
NP-5	46		9/4/02		3.06	0.91	0.10			13 7.3					
NP-6	51	mpnse,fatigue,fibroids,bleeding	7/26/02		1.67				7.2	1.20 42 30	7.91 bleeding on cycHRT(7/26?)				
	-	-	9/17/02			0.65	-0.16				st ST4 50 9/30, improved 10/2	0.2		0.75	
	-	-	8/8/95							47 105	on prepro5(7/16?)				
	-	-	8/8/02							0.75	prepro start?				
NP-7	-	afib,MVA,pneumonia,vagbld	9/1/02		7.35	0.51	-0.30		1.9		MVA(1wk), stop prepro,heparin,+BCstaph				
	-	cx polyp	9/7/02						7.4		NSR on ST4 50 (9/2),restart prepro,cr=2		1.6		
NP-8	50	menpse,lregMense,SVT	8/22/02		4.85	0.96	0.15			100 80					
NP-9	46	lregMenses	9/4/04		2.40	0.95	0.14								
NP-10	50	fibroids,chrnpain,fatigue,anemia,constp,hair	7/30/02		5.01	0.68	-0.13				st LT4 25,BV,b12=326,fol nl(macrocytes on pap)	4.22	0.79		
	-	-	8/29/02							5.4 3.7	atrophic cx, prolif endom(7/24),Uincont				
NP-11	64	++hthsxs,brst cysts,numbness	9/9/02		2.59	0.73	-0.08				TVH,startcycHRT,st LT4 25(9/19),rpt6mo				
NP-12	54	menpse,hth sx's,ov cyst,BV	10/2/02		5.61	0.99	0.18			68 42	bellpalsy,strtprmpse, imprvd/st 25(10/2)	0.61	1.3		
	65	PMB,fibroids,weak,BV	10/1/02								maintenance125,Aygestin5bid				
NP-13	66	menpse sxs,kidstn,hrtvlv REPL	9/23/03		4.79	0.81	0.00			63 28	constp,insomnia,premphase9/30,0.075(9/30)				
NP-14	24	(4wks PP) recurSAB	08/30/02	4wPP	3.46	0.97	0.16			1 0.8	sx,recurBV				
	-	(8wks PP) anovulation	09/26/02	8wPP						2.2 9.1	start LT4 50,-ACA	5.96	0.87		
					STDevdiff= 0.15										
<b>NON-PREG AVERAGE</b>			<b>TSH/FT4</b>	<b>4.6</b>	<b>3.71</b>	<b>0.81</b>			<b>7.3</b>						
(WITH PROBLEMS)			STDev	1.95	0.15										

PREGNANT vs NON-PREGNANT (WITH PROBLEMS) COMPARISON														
NAME	AGE	DX	TSH/FT4	TSH	FT4	FT3	TT4	T3 UPFSH LH	OTHER COMMENTS	TSH's	FT4's	T3U's	TT4	
				.49-4.67	.71-1.85	2.3-4.2	4.5-12.0	.6-1.27 0-20 0-20						
<b>PREGNANT AVERAGE</b>			<b>3.3</b>	<b>2.53</b>	<b>0.76</b>		<b>9.6</b>							
<b>NON PREG AVERAGE</b>			<b>4.6</b>	<b>3.71</b>	<b>0.81</b>		<b>7.3</b>							
<b>PREG+NON AVERAGE</b>			<b>3.9</b>	<b>3.03</b>	<b>0.78</b>		<b>9.0</b>	0.17						
<b>PREG-NON DIFFERENCE</b>			<b>-1.3</b>	<b>-1.18</b>	<b>-0.05</b>		<b>2.3</b>	2.53						
[Preg<20wk-NON] DIFF			<b>0.3</b>	<b>0.33</b>	<b>0.13</b>		<b>-1.6</b>		<20 weeks HCG effect maintains FT4?					
[Preg>20wk-NON] DIFF**			<b>-1.8</b>	<b>-1.77</b>	<b>-0.12</b>		<b>3.5</b>							
[Preg<20wk->20wk] DIFF =			<b>1.5</b>	<b>2.10</b>	<b>0.25</b>		<b>-5.1</b>							
[PregTSH<2-NON] DIFF		[<2-NON] =	<b>-2.4</b>	<b>-2.41</b>	<b>-0.11</b>		<b>3.1</b>							
[PregTSH>2-NON] DIFF		[>2-NON] =	<b>0.3</b>	<b>0.35</b>	<b>0.02</b>		<b>1.4</b>							

Table 1 non-pregnant

TABLE 2 Non-Pregnant Problem Patients

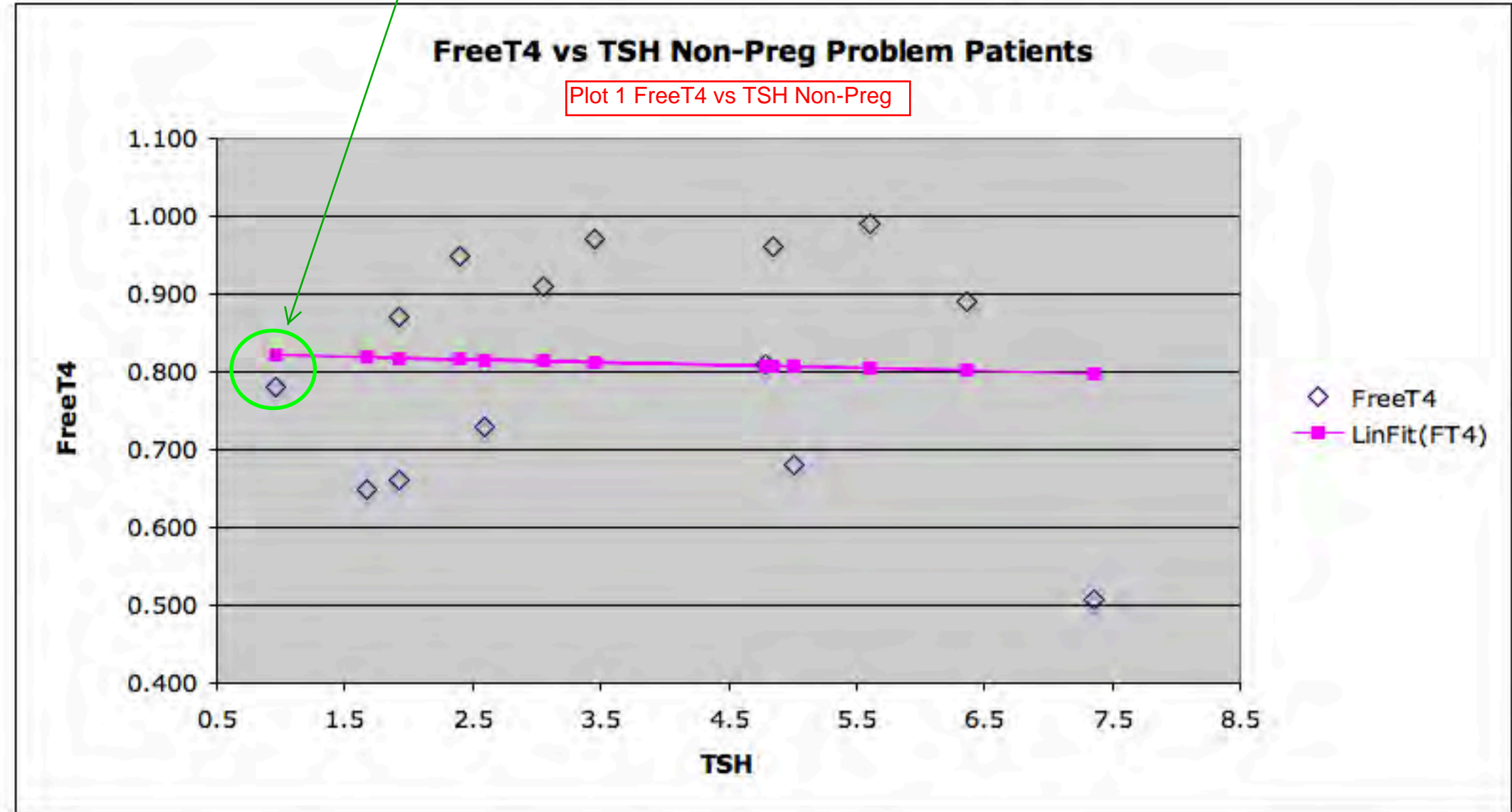
Above is the tabulation of patients with clinical problems, lab values and treatment comments. Averages and Differences for patients 20-41 weeks of Pregnancy and Non-Pregnancy are calculated. Five additional patients at 4-8 weeks Gestation (presenting with spontaneous miscarriage) are also tabulated.

Table 1,2 Description



	TSH	FreeT4	LinFit(FT4)	
1	7.35	0.506	0.798	-0.292
	1.67	0.650	0.819	-0.169
	1.93	0.660	0.818	-0.158
	5.01	0.680	0.806	-0.126
	2.59	0.730	0.815	-0.085
	0.96	0.780	0.821	-0.041
	4.79	0.810	0.807	0.003
	1.92	0.870	0.818	0.052
	6.36	0.890	0.802	0.088
	3.06	0.910	0.814	0.096
	2.40	0.950	0.816	0.134
	4.85	0.960	0.807	0.153
	3.46	0.970	0.812	0.158
14	5.61	0.990	0.804	0.186

Correl= -0.047902  
 $t=r*\sqrt{(n-2)/(1-r*r)}$  = -0.16613  
 FreeT4avg= 0.811



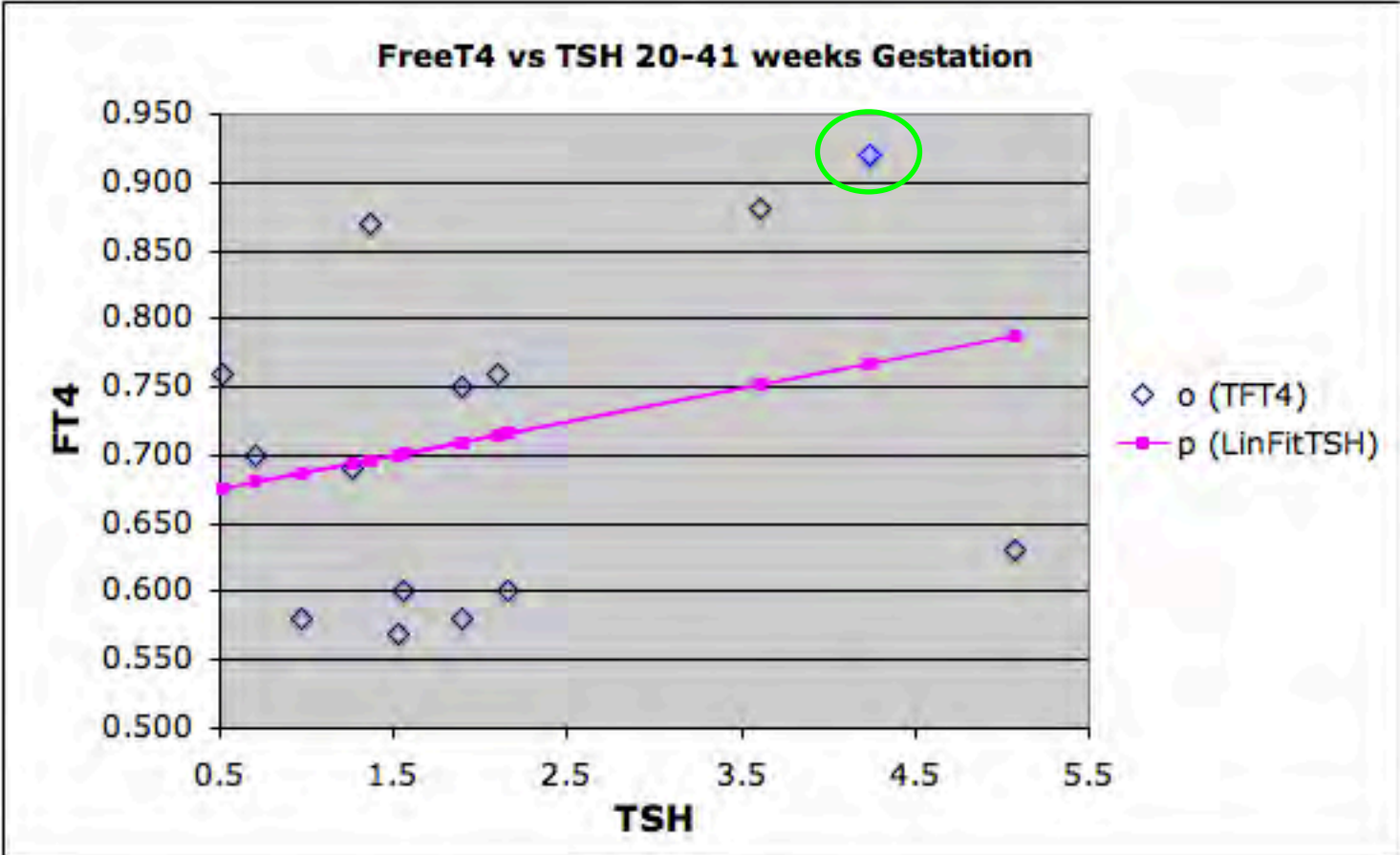
$$\text{FreeT4} = 0.825 - 0.004 * \text{TSH}$$

from TSH = 1 setpoint

from delta TSH modulation about setpoint

	F (TSH)	o (TFT4)	p (LinFitTSH)
34	1.52	0.570	0.701
32	1.9	0.580	0.710
37	0.97	0.580	0.687
27	1.56	0.600	0.702
40	2.16	0.600	0.716
35	5.08	0.630	0.787
32	1.26	0.690	0.694
33	0.70	0.700	0.681
32	1.90	0.750	0.710
29	0.51	0.760	0.676
40	2.10	0.760	0.715
34	1.37	0.870	0.697
20	3.61	0.880	0.751
41	4.24	0.920	0.767

correl= 0.284337  
 $t=r*\sqrt{(n-2)/(1-r*r)} = 1.027377$   
 FreeT4avg= 0.706



Plot2

PLOT 2,3  
 FreeT4 vs TSH > 20 weeks

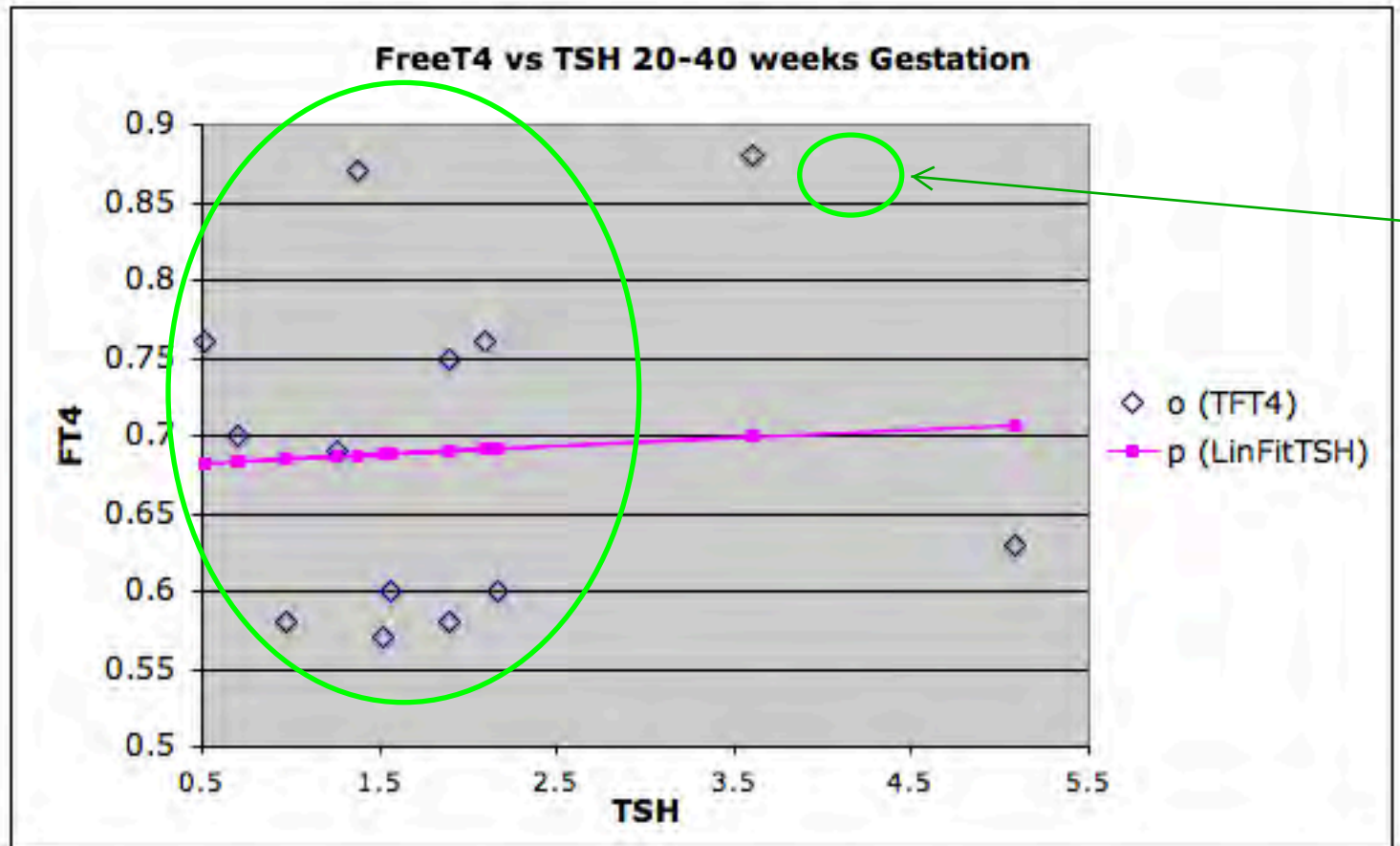
Free T4 vs TSH All Patients

Free T4 = 0.664 + 0.024 \* TSH

equilibrium?

	F (TSH)	o (TFT4)	p (LinFitTSH)
34	1.52	0.570	0.688
32	1.9	0.580	0.690
37	0.97	0.580	0.685
27	1.56	0.600	0.688
40	2.16	0.600	0.691
35	5.08	0.630	0.707
32	1.26	0.690	0.687
33	0.70	0.700	0.684
32	1.90	0.750	0.690
29	0.51	0.760	0.683
40	2.10	0.760	0.691
34	1.37	0.870	0.687
20	3.61	0.880	0.699

correl= 0.061398  
 $t=r*\sqrt{(n-2)/(1-r*r)} = 0.20402$   
 FreeT4avg= 0.690



Plot3

Free T4 vs TSH Omitting 41 week patient

Free T4 = 0.680 + 0.005 \* TSH

Shown above is FreeT4 vs TSH for the Non-Pregnant, and Pregnant patients at 20-41 weeks.  
Regression lines are shown, and no significant correlation is noted (particularly for TSH < 2.0).

Plot2,3 Description

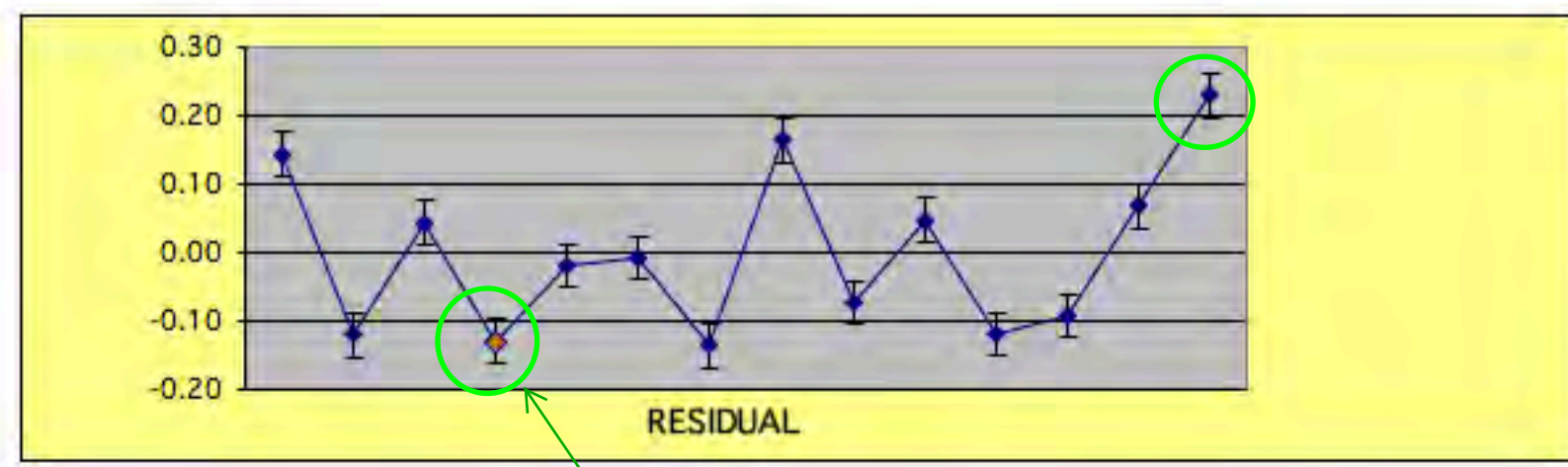
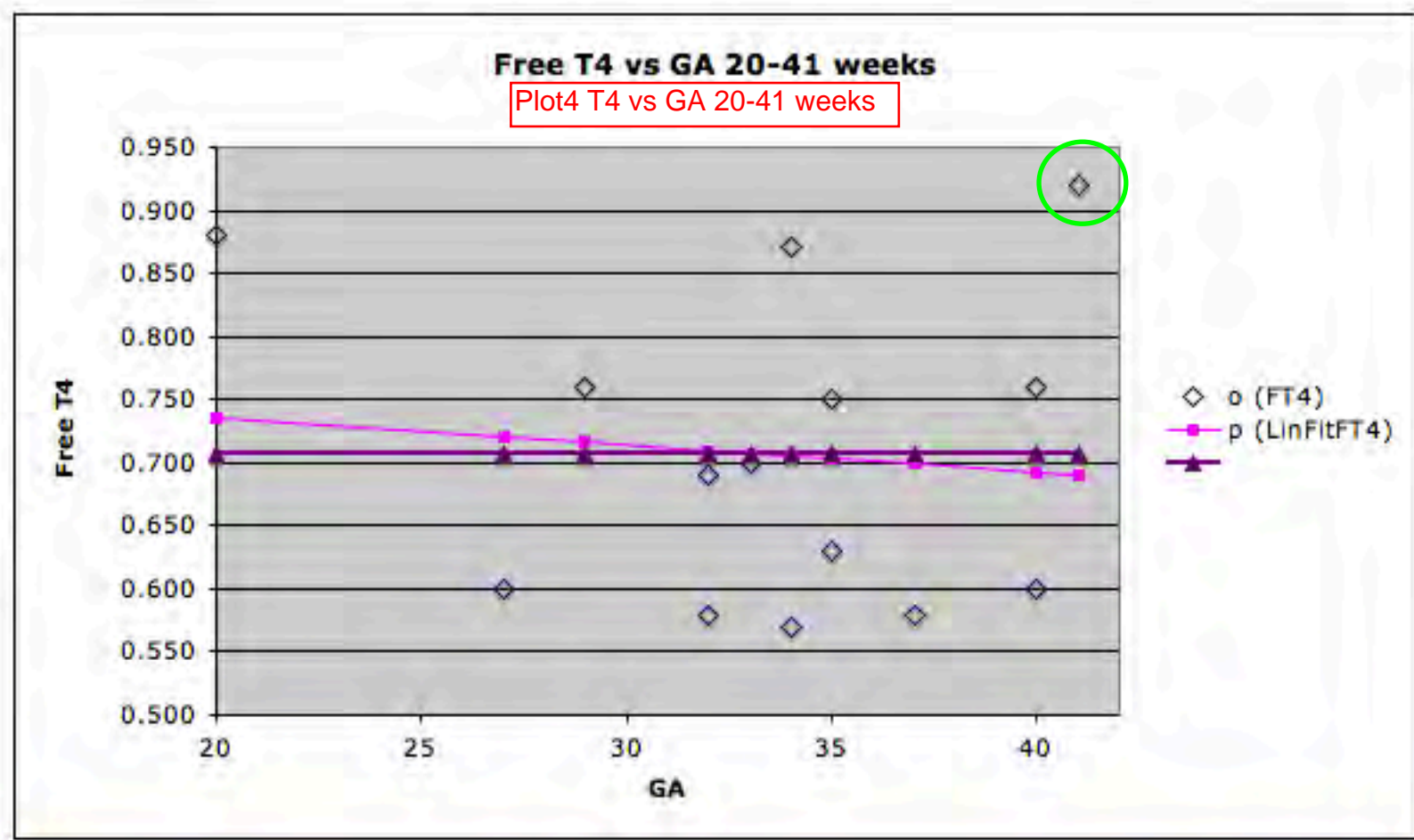


	F (GA)	o (FT4)	p (LinFitFT4)	
1	20	0.880	0.736	0.706
	27	0.600	0.721	0.706
	29	0.760	0.716	0.706
	32	0.580	0.710	0.706
	32	0.690	0.710	0.706
	33.00	0.700	0.708	0.706
	34.00	0.570	0.705	0.706
	34.00	0.870	0.705	0.706
	35.00	0.630	0.703	0.706
	35.00	0.750	0.703	0.706
	37.00	0.580	0.699	0.706
	40.00	0.600	0.692	0.706
	40.00	0.760	0.692	0.706
14	41.00	0.920	0.690	0.706

correl= -0.10184  
t=r\*sqrt[(n-2)/(1-r\*r)] = -0.35464

FreeT4avg= 0.706

Free T4 = 0.780 - 0.002 \* TSH  
constant

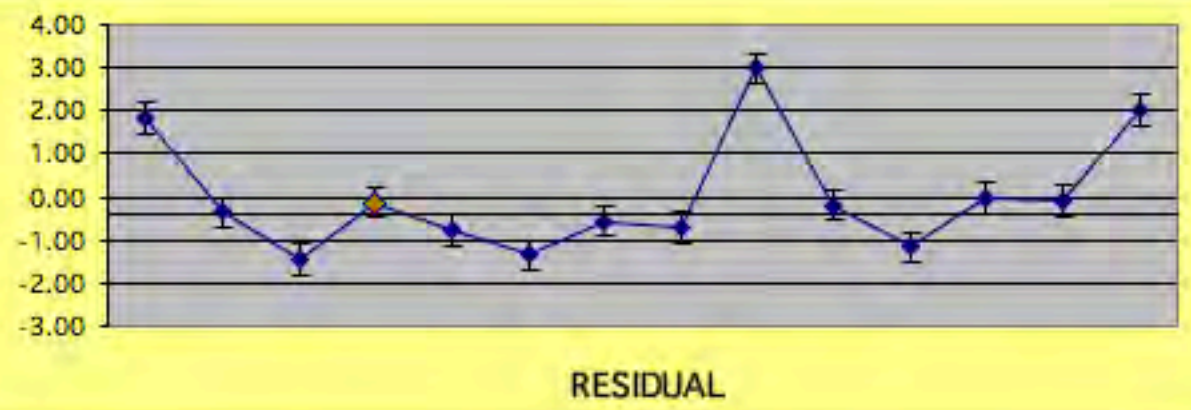
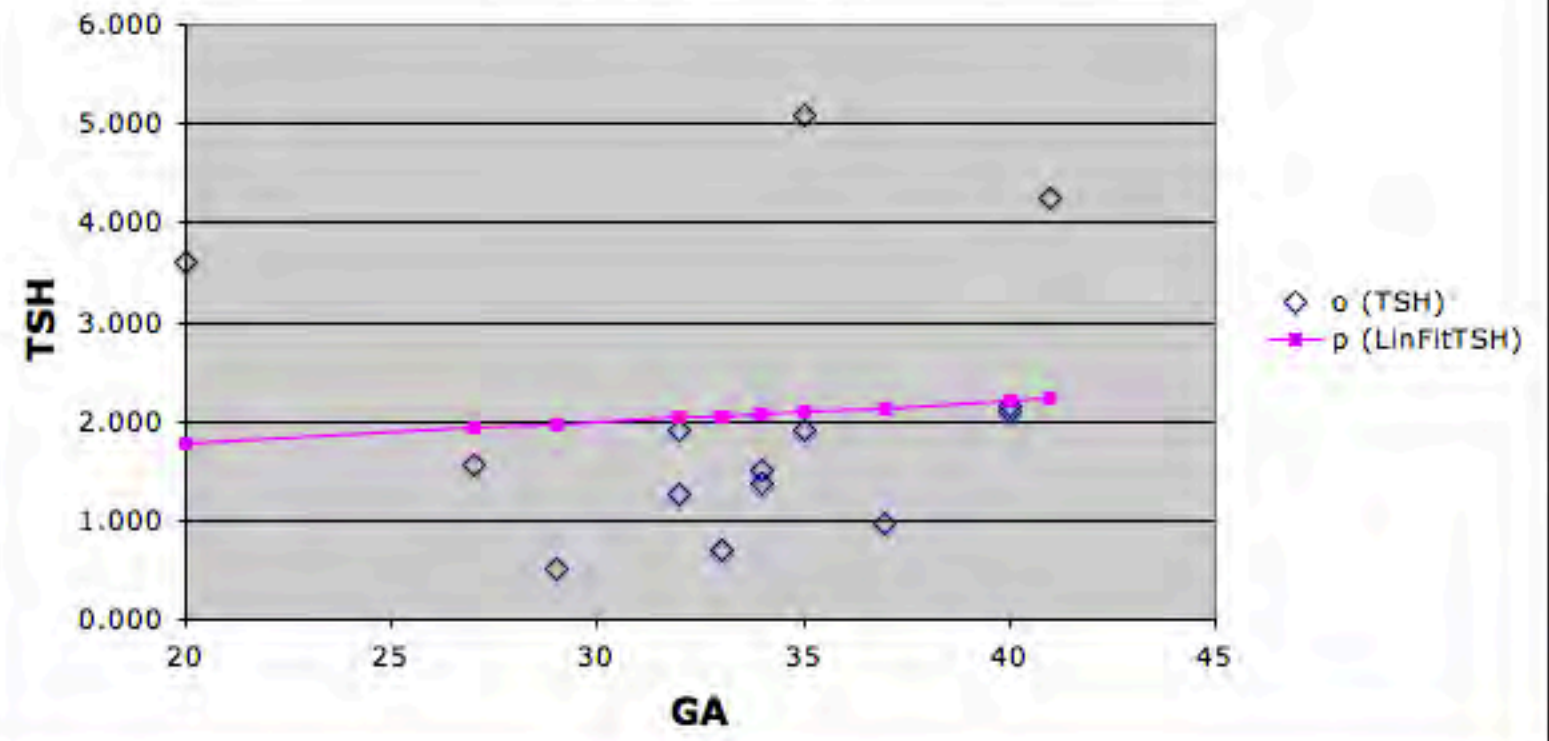


	F (FT4)	o (TSH)	p (LinFitTSH)
1	20	3.610	1.780
	27	1.560	1.927
	29	0.510	1.969
	32	1.900	2.031
	32	1.260	2.031
	33.00	0.700	2.052
	34.00	1.520	2.073
	34.00	1.370	2.073
	35.00	5.080	2.094
	35.00	1.900	2.094
	37.00	0.970	2.136
	40.00	2.160	2.199
	40.00	2.100	2.199
14	41.00	4.240	2.220

correl= 0.087  
 $t=r*\sqrt{(n-2)/(1-r^2)}$  0.277  
 TSHavg= 2.063

### TSH vs GA >20-41 weeks

Plot 5 TSH VS GA >20-41



Plot 5 TSH VS GA >20-41Description

Above is the Plot of FreeT4 and TSH vs Gestational Age (GA) for 20-41 weeks of Pregnancy with regressions lines. No significant correlation is noted for either with Gestational Age, and the data is well represented by the Mean values.

not important for

In an effort to better understand these findings, a regression fit was performed including early pregnancies 4-8 weeks. They represent Spontaneous Miscarriages. When these are included, the regression from 2-41 weeks indicates a global decrease in FreeT4 with Gestational Age from early to late pregnancy, contrary to the findings for 20-41 weeks, and consistent with reports in the literature. below

Plot 6 FT4 vs GA 4-41 weeks Preg Description



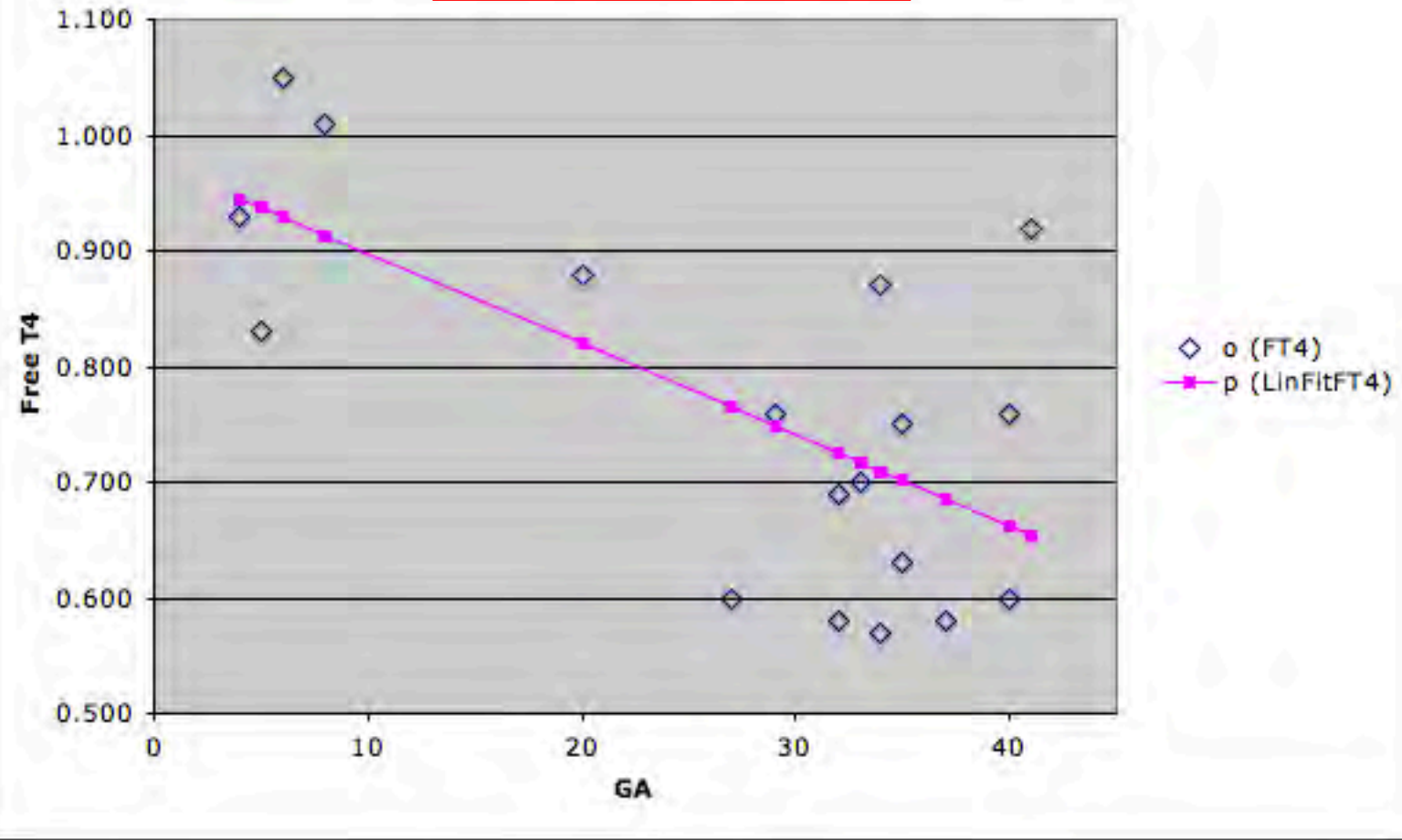
GA	o (FT4)	p (LinFitFT4)
4	0.930	0.945
5	0.830	0.937
6	1.050	0.929
8	1.010	0.913
20	0.880	0.819
27	0.600	0.764
29	0.760	0.749
32	0.690	0.725
32	0.580	0.725
33.00	0.700	0.717
34.00	0.570	0.709
34.00	0.870	0.709
35.00	0.630	0.701
35.00	0.750	0.701
37.00	0.580	0.686
40.00	0.760	0.662
40.00	0.600	0.662
41.00	0.920	0.654

correl= -0.64994  
 t=r\*sqrt[(n-2)/(1-r\*r)] = -2.96254

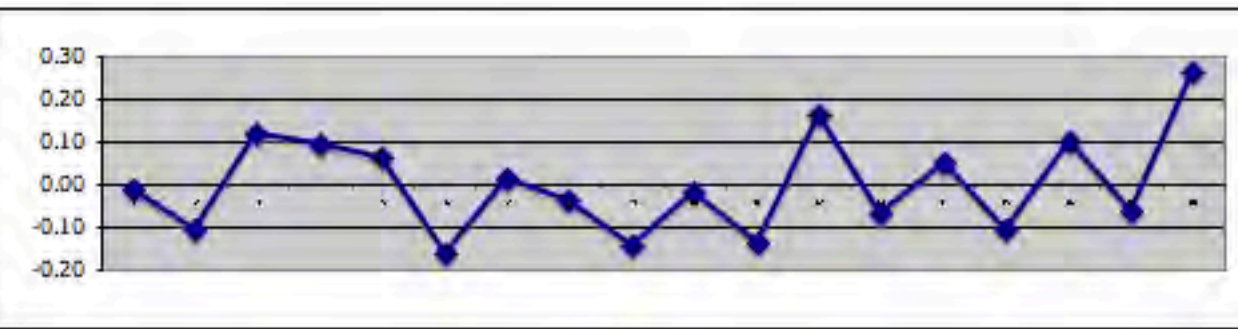
FreeT4avg= 0.762

### FT4 vs GA Pregnancy 4-41 weeks

Plot 6 FT4 vs GA 4-41 weeks Preg



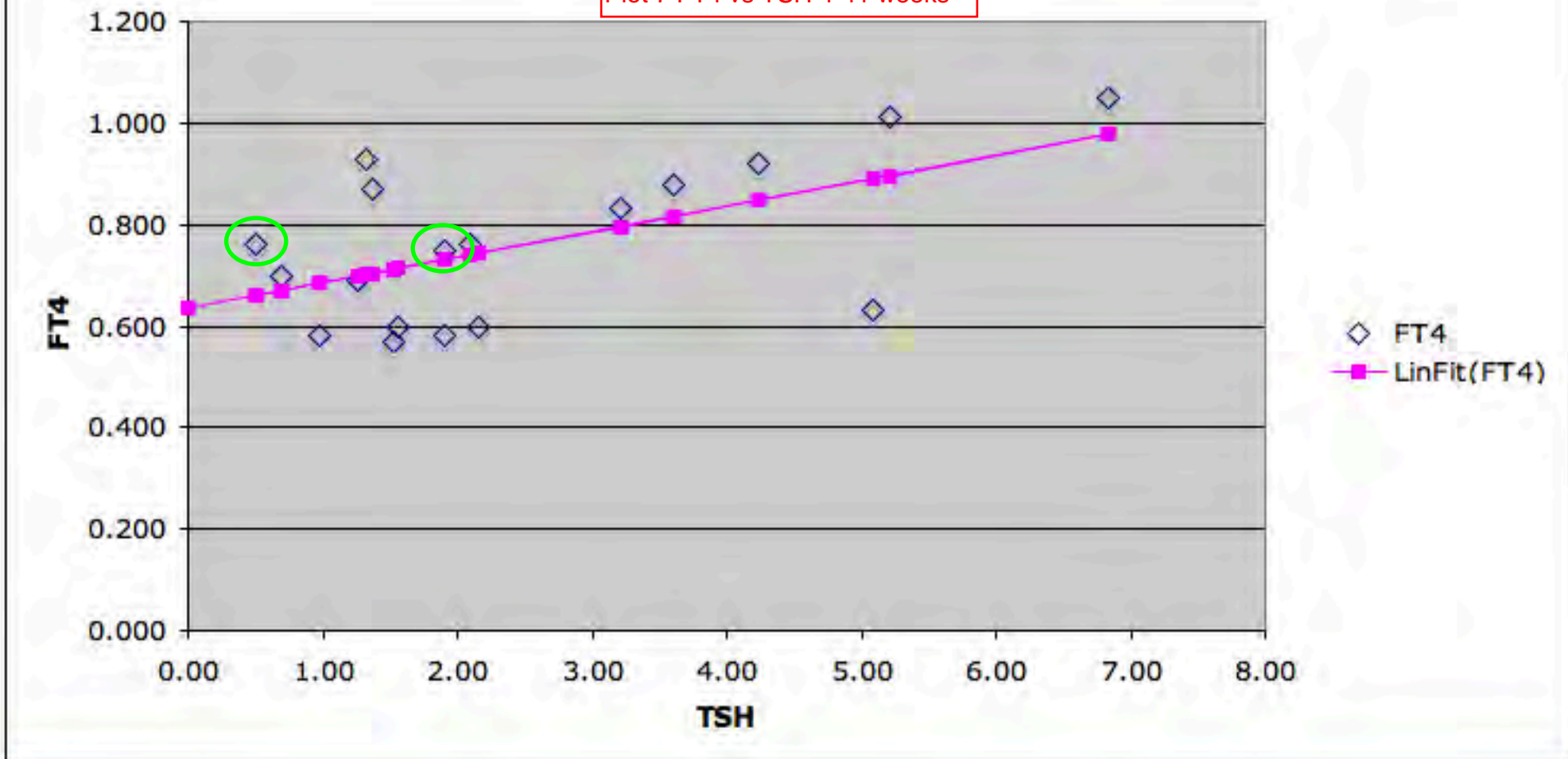
Free T4 = 0.000785 - 0.008 \* TSH





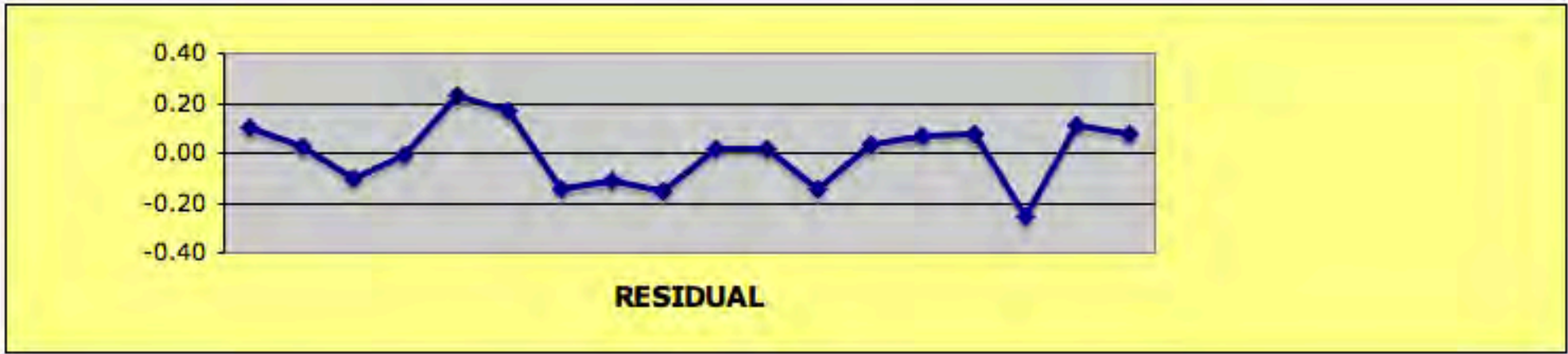
### FreeT4 vs TSH 4-41 weeks

Plot 7 FT4 vs TSH 4-41 weeks



GA	TSH	FT4	LinFit(FT4)
4	0.51	0.760	0.661
5	0.7	0.700	0.670
6	0.97	0.580	0.684
8	1.26	0.690	0.698
20	1.32	0.930	0.701
27	1.37	0.870	0.704
29	1.52	0.570	0.711
32	1.56	0.600	0.713
32	1.9	0.580	0.730
32	1.9	0.750	0.730
33	2.1	0.760	0.740
34	2.16	0.600	0.743
34	3.22	0.830	0.796
35	3.61	0.880	0.816
37	4.24	0.920	0.847
40	5.08	0.630	0.889
40	5.22	1.010	0.896
41	6.84	1.050	0.978
	0		0.635

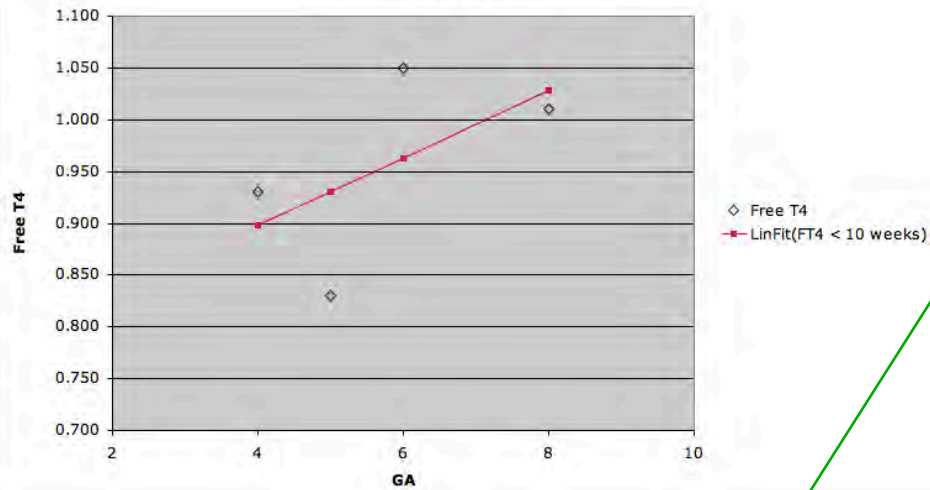
correl= 0.5756  
 $t=r*\sqrt{(n-2)/(1-r^2)}$  = 2.4385  
 FreeT4avg= 0.762



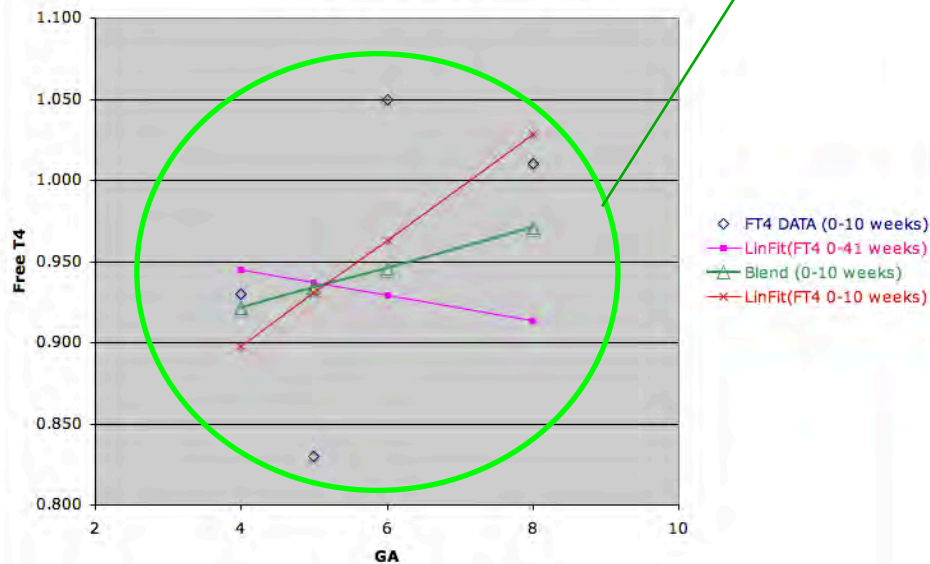
However, a finer look at the data by graphing the Linear Fit <10 weeks Pregnancy with the Linear Fit >20 weeks produces a plot which simulates the data, noting a break at 15 weeks, shown below [Blend Fit]:

# Free T4 vs GA 0-41 weeks Blend Fit

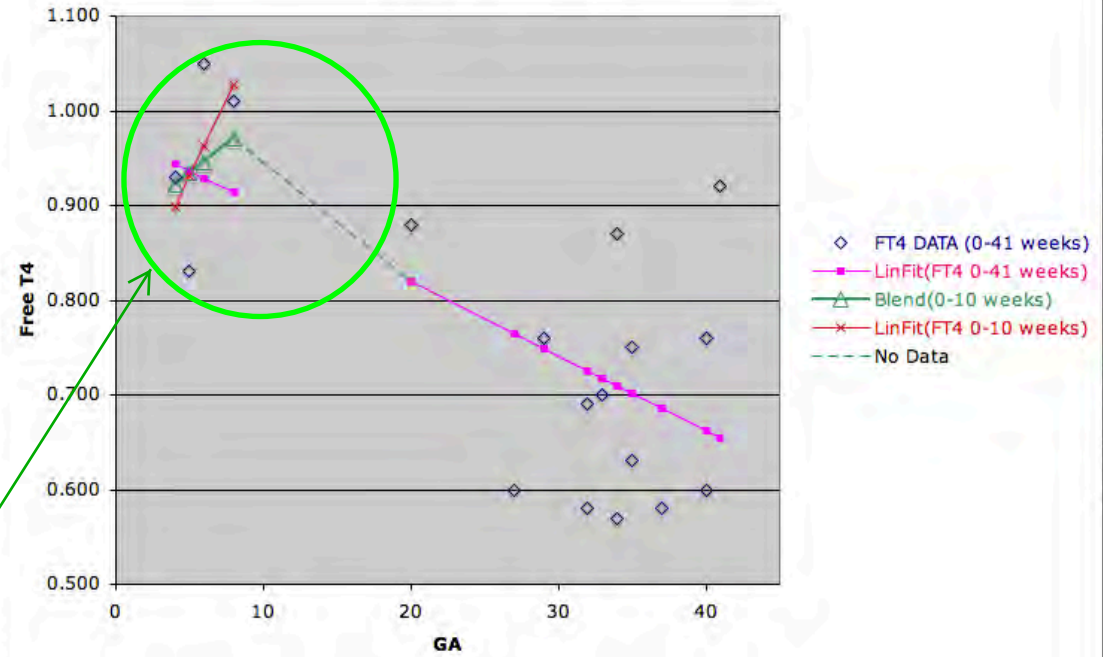
### Free T4 vs GA 0-10 weeks



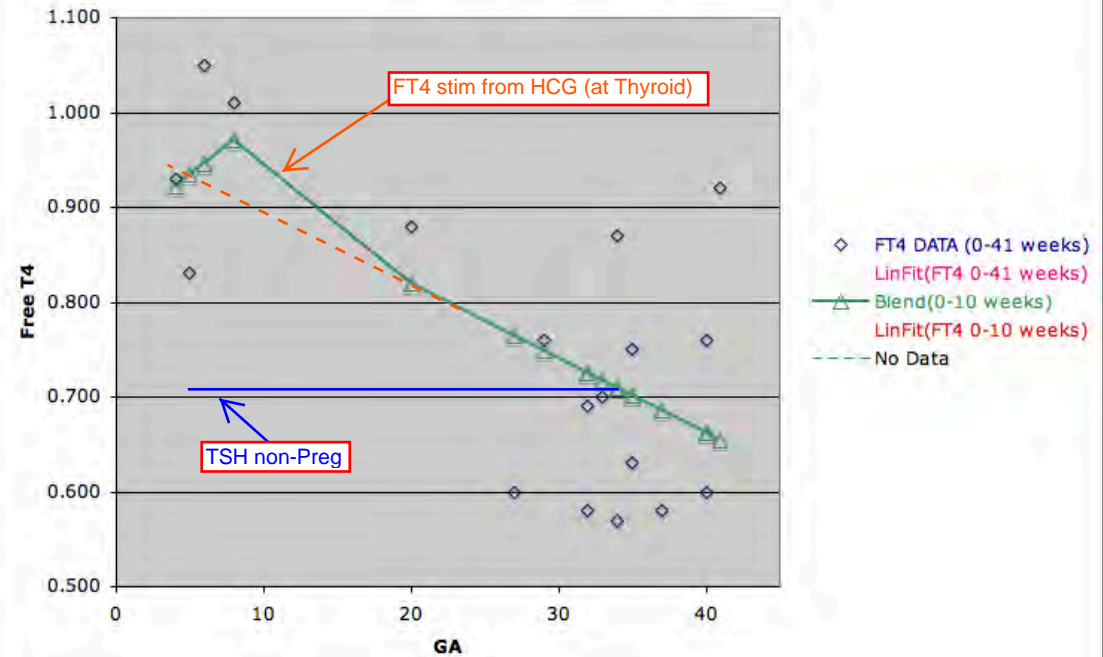
### FT4 vs GA 0 - 10 weeks Blend Fit



### FT4 vs GA Blend Fit Pregnancy



### FT4 vs GA Blend Fit Pregnancy



# Estimation of HCG Stimulation of Free T4 in Early Pregnancy

TSH 0.8 to 1.4  
Of 0.6 = .04 FreeT4

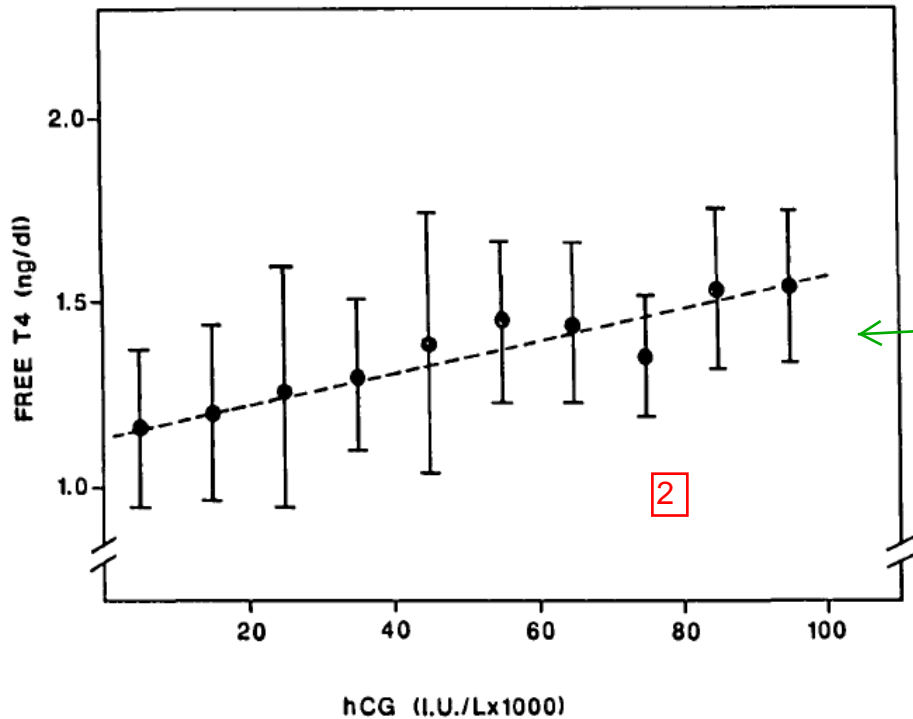


FIG. 7. Scattergram of free T<sub>4</sub> in relation to hCG concentrations. Each point represents the mean (±1 SD) free T<sub>4</sub> value, determined between 6-20 weeks gestation, for 10,000 IU/L increments in hCG. The dashed line indicates the linear regression curve.

Free T4 is linear with HCG  
in Early Pregnancy

$$\text{Free T4 Stim} = (1.5-1.2) / (1 \times 10^{-5} * [\text{HCG}])$$

$$= 3 \times 10^{-6} * \text{HCG}$$

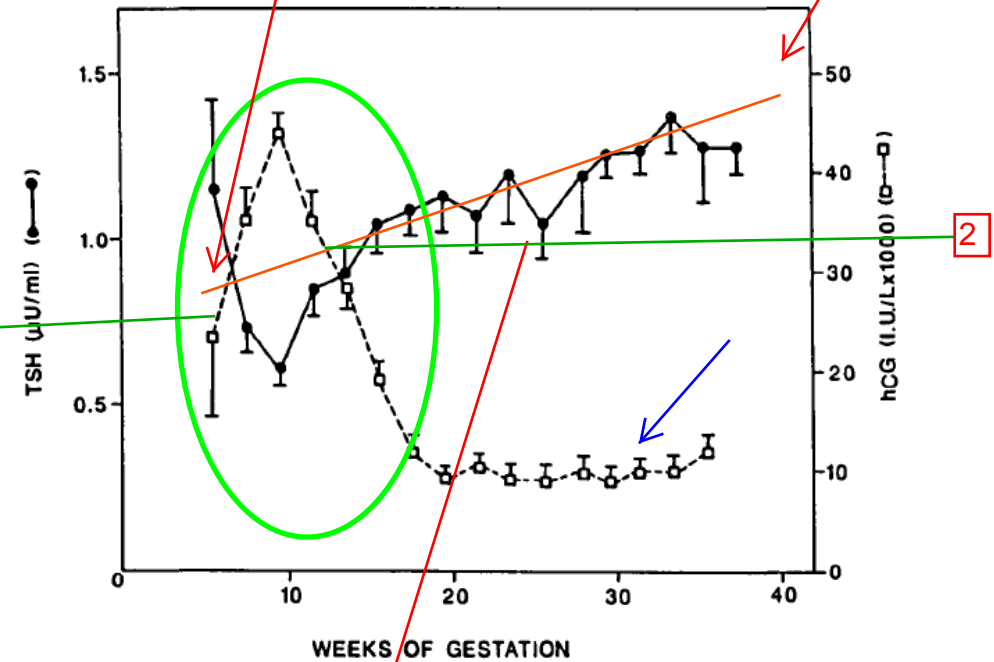


FIG. 6. Serum TSH and hCG as a function of gestational age. Serum hCG was determined at initial evaluation, and TSH at initial evaluation and during late gestation. The symbols give the mean value (±SE) for samples pooled for 2 weeks of gestation. Each point corresponds to the average of 33 determinations for hCG and 49 for TSH.

HCG changes with GA, peaking at  
10 weeks, and decreasing to  
a constant after 20 weeks

(adapted from Glinoe et al 1990)

$$\text{FreeT4 (preg)} = 0.2 - .06\text{TSH}$$

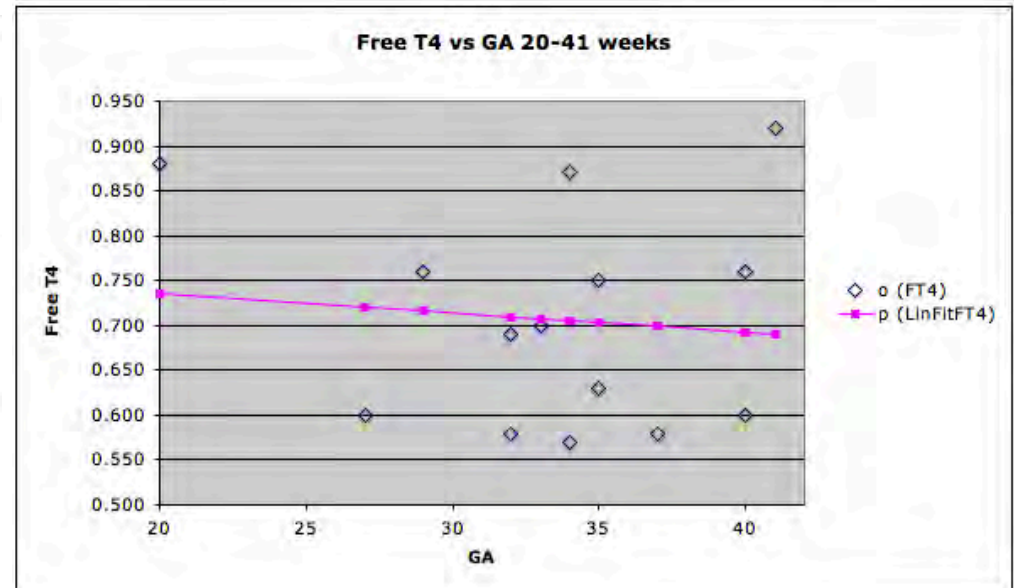
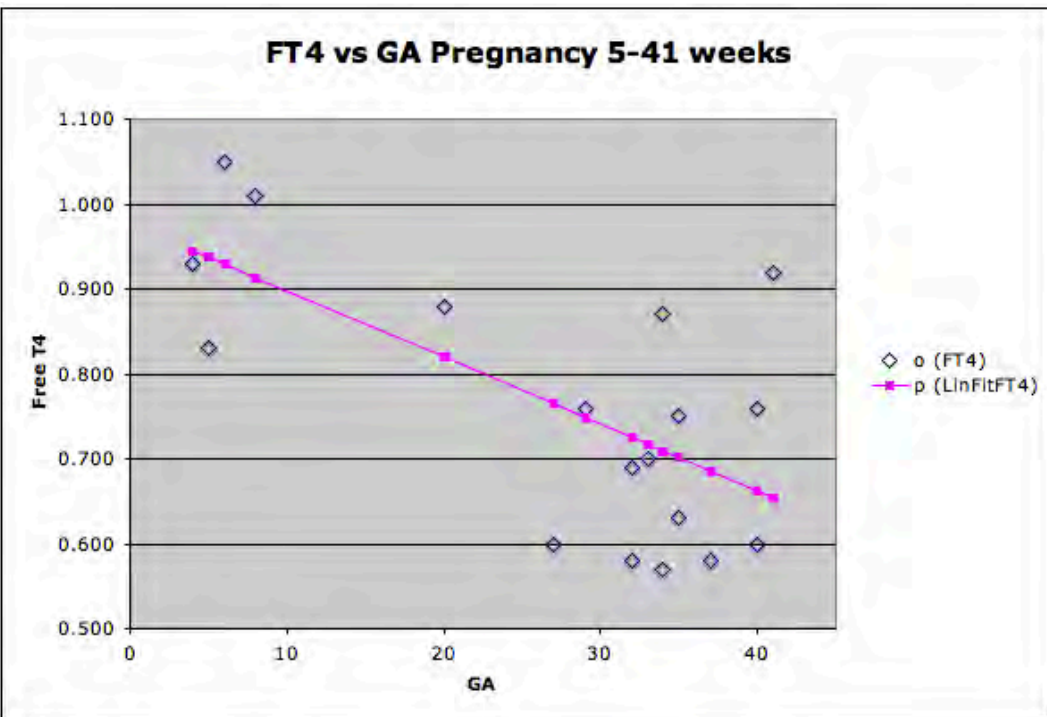
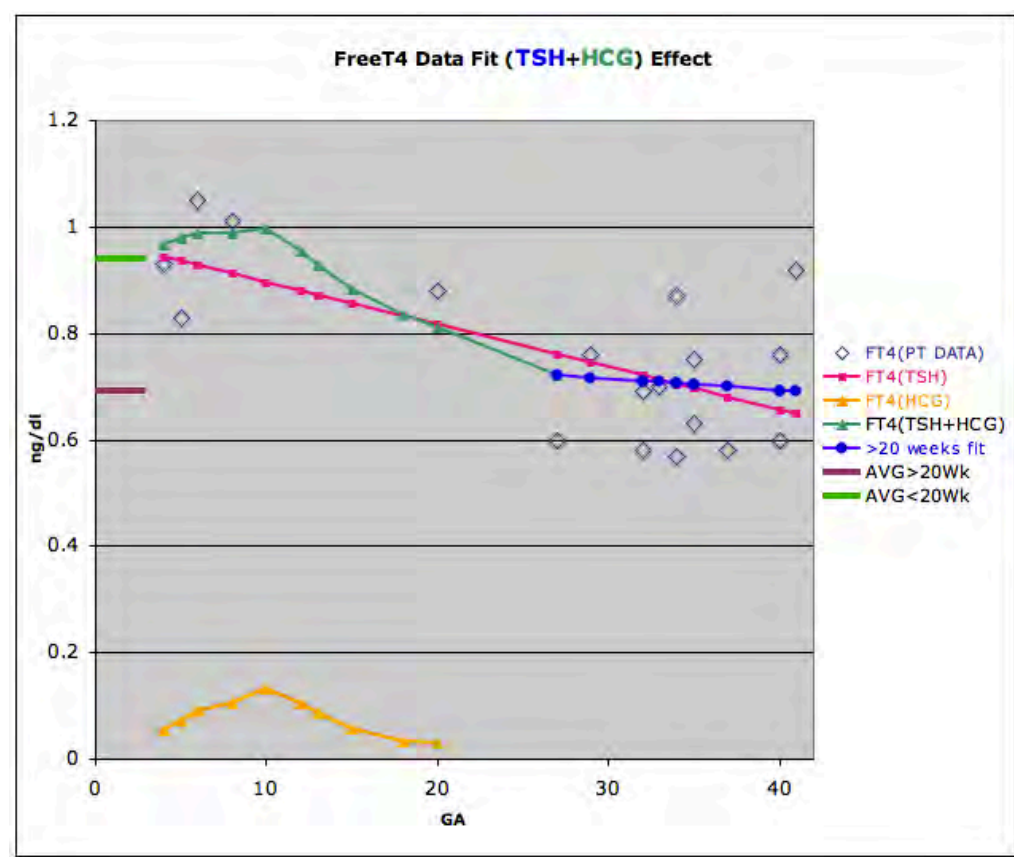
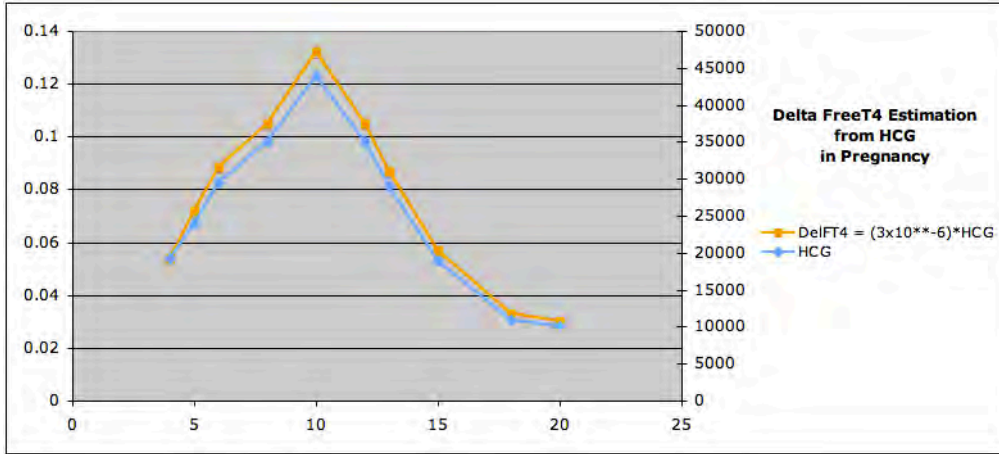
FreeT4 in Early Pregnancy is noted to have a linear relationship with HCG (Glinoeer 1990, J. Clin. Endocrinol. Metab. 1990 71: 276-287). From this an expected change in FreeT4 =  $(1.5-1.2) \times 10^{-5} = [3 \times 10^{-6} * \text{HCG}]$  can be estimated. Using the HCG change as a function of Gestational Age, an expected change in FreeT4 with Gestational Age can be estimated. This calculation is plotted below.



# Estimation of Free T4

## Adding HCG Stimulation < 20 weeks

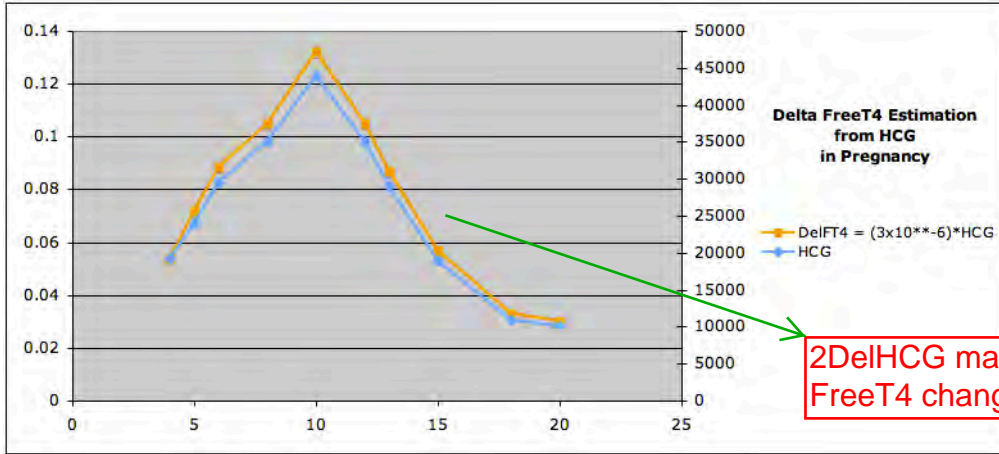
Free T4 Linefit + HCG Stim (0-20 weeks)  
 Free T4 Linefit (20-41 weeks)



# Estimation of Free T4

## Adding HCG Stimulation < 20 weeks

Free T4 Linefit + HCG Stim (0-20 weeks)  
 Free T4 Linefit (20-41 weeks)



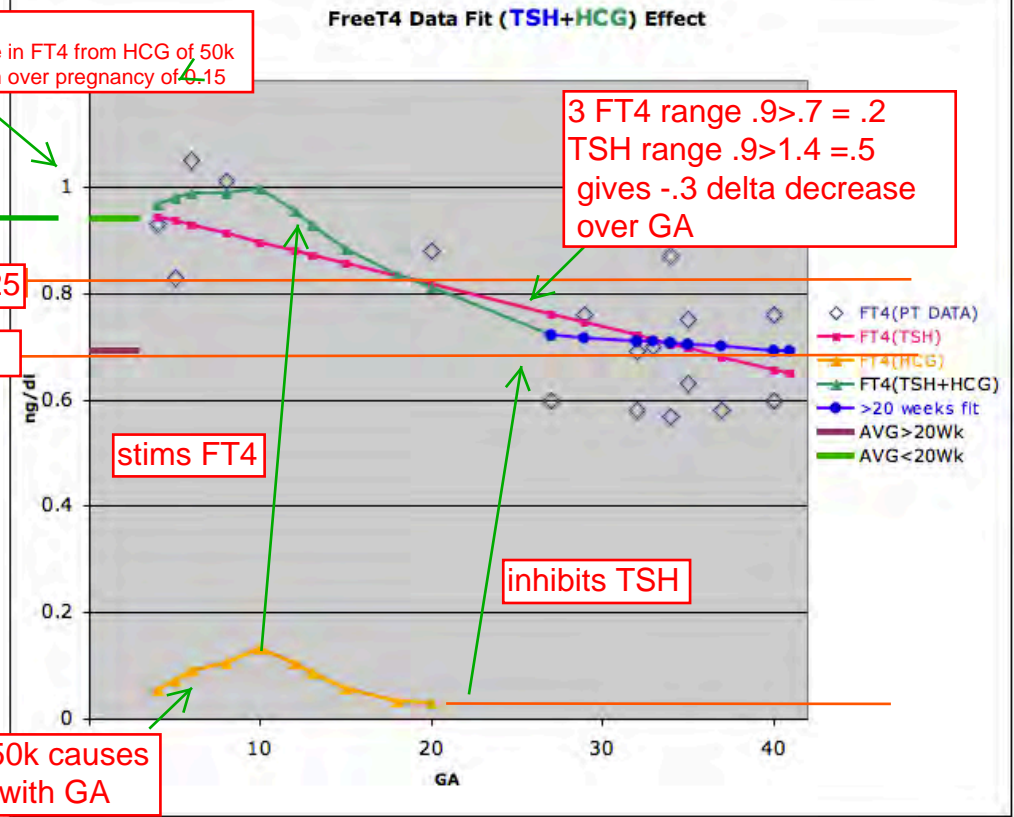
$\text{FT4} = -\log\text{TSH}$

$1\text{NP} = 0.825$

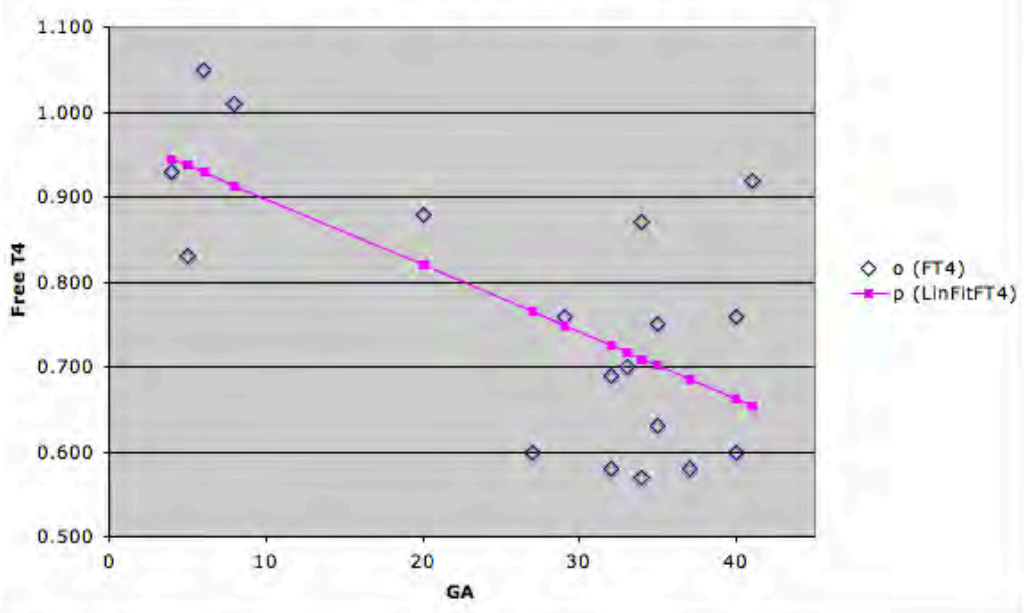
$4\text{delP} = -0.1$

2DelHCG max 50k causes FreeT4 change with GA

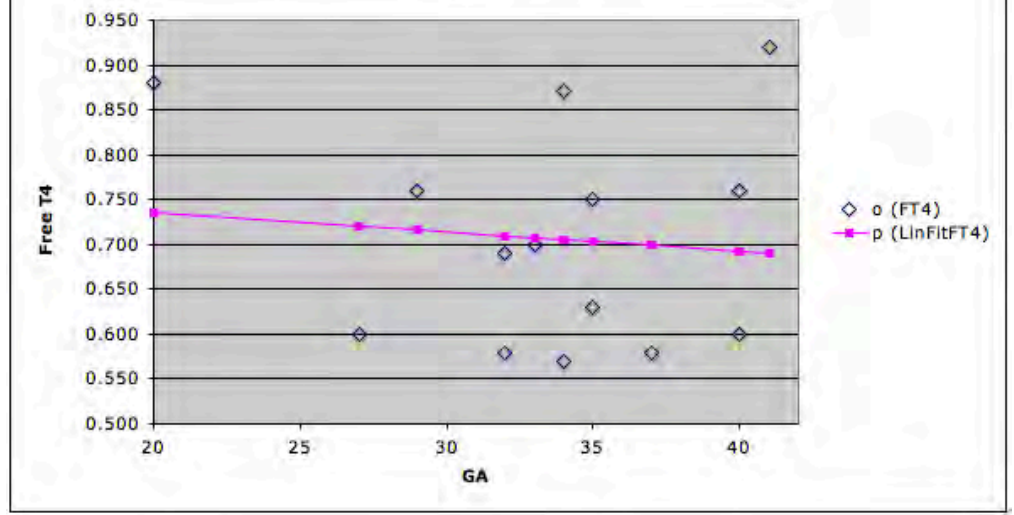
5 Preg = 1  
 shift increase in FT4 from HCG of 50k constant stim over pregnancy of 0.15



### FT4 vs GA Pregnancy 5-41 weeks



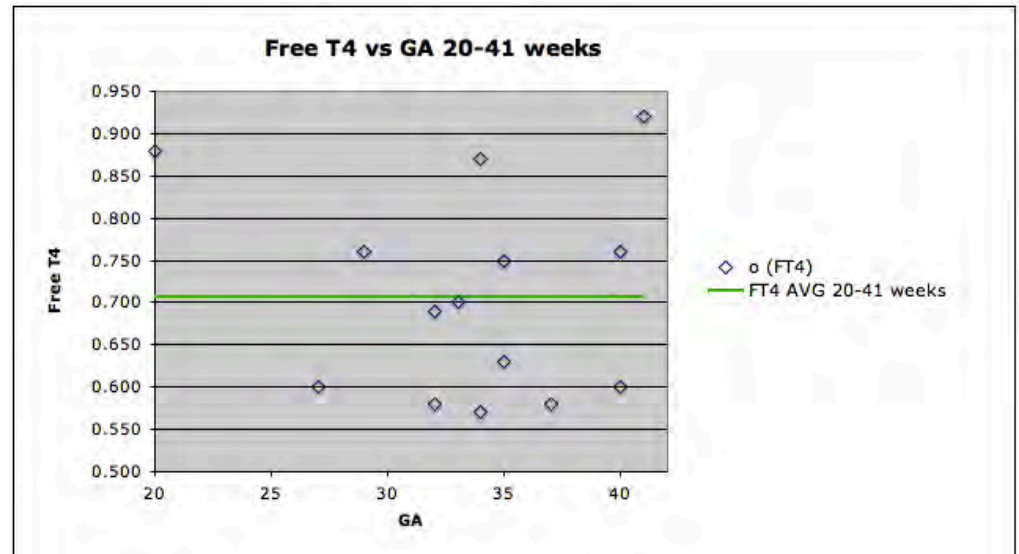
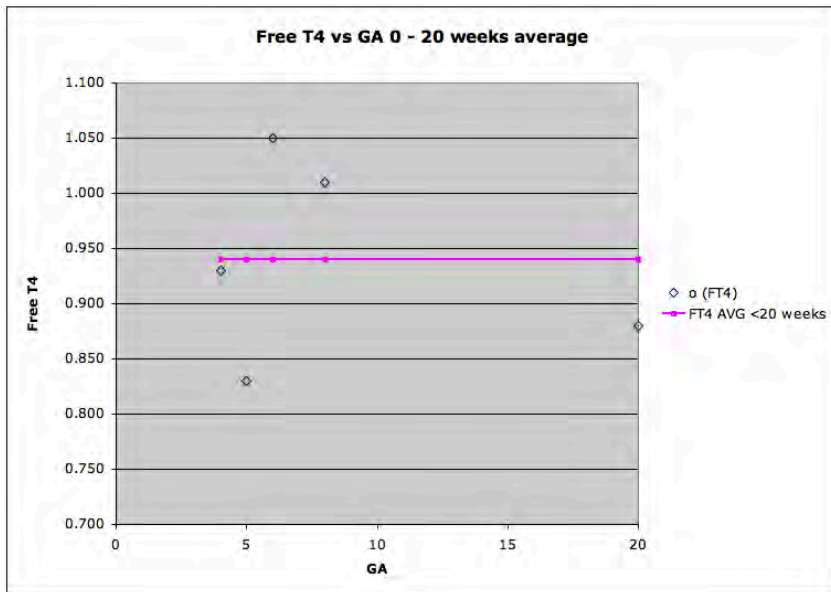
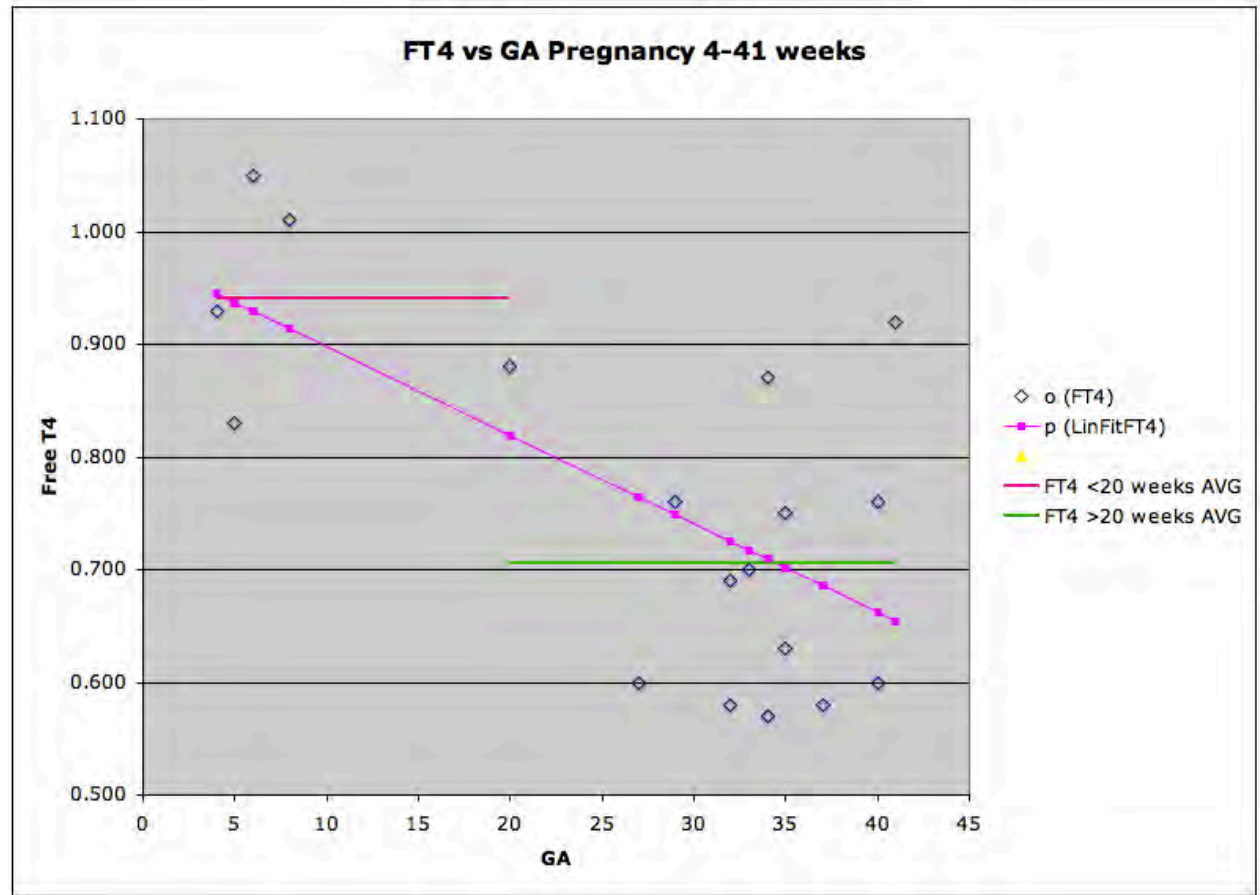
### Free T4 vs GA 20-41 weeks



The above left graph is the estimated change in FreeT4 due to HCG in early pregnancy. When this is added to the global regression fit from 2-41 weeks, the result is a graph that approximates the data <20 weeks. This is shown at the top right above, combined with the values from the linear fit for 20-41 weeks previously shown (lower right above).



# Free T4 vs GA Pregnancy Split Fit at 20 weeks



The graph above plots the average FreeT4 for 2-20 weeks and 20-41 weeks with the patient data. Note that the difference in the means is  $\sim 0.23$  ng/dl. This may provide a useful simplified approach to evaluating and treating pregnant patients with thyroid dysfunction.

The graph above plots the average FreeT4 for 2-20 weeks and 20-41 weeks with the patient data. Note that the difference in the means is  $\sim 0.23$  ng/dl. This may provide a useful simplified approach to evaluating and treating pregnant patients with thyroid dysfunction.

## CONCLUSION

The data presented supports the idea that FreeT4 levels in Pregnancy may be modeled by the contributions of several components:

$$\begin{aligned} \text{FreeT4Pregnancy} = & \boxed{1} \text{FreeT4NonPreg} & \boxed{= +.9 \text{ ng/dl} = (-.06)(\log\text{TSH}) \text{ Setpoint at Pituitary}} \\ & \boxed{4} + \text{TSHstim} & \boxed{= +0.2 \text{ ng/dl} = (-\log\text{TSH}) \text{ Setpoint at Pituitary}} \\ & \boxed{2} + \text{HCGsuppress} & \boxed{= - \text{TSH DelPreg setpoint at Pituitary}} \\ & \boxed{3} + \text{HCGstim} & \boxed{= -0.2 \text{ from HCG suppress}} \\ & \boxed{5} + \text{FreeT4suppress} & \boxed{= +.2 \text{ ng/dl (HCG on Setpoint at Thyroid)}} \\ & & \boxed{= -0.06 \text{ (FT4 suppress at Pituitary)}} \end{aligned}$$

FreeT4NonPreg = Free Thyroxine Levels of the non-pregnant patient

TSHstimulation = TSH stimulation of FT4 (?Pituitary)

TSHsuppression = HCG suppression of TSH (?Pituitary)

HCGstim = HCG stimulation of FreeT4 (?Thyroid)

Special thanks to Duncan Ferguson, PhD  
University of Illinois, Urbana, USA