



The 11th Diczfalusy Award Lecture Symposium on Reproductive Health

The effect of delivery method on secretion pattern and dissociation phenomenon of adrenocorticotrophic hormone and cortisol in parturients



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Orastie, 6th October 2017

General adaptation syndrome

- Increased heart rate
- Increased blood pressure
- Deeper breathing
- Muscular strength
- Increased glycaemia
- Better perception

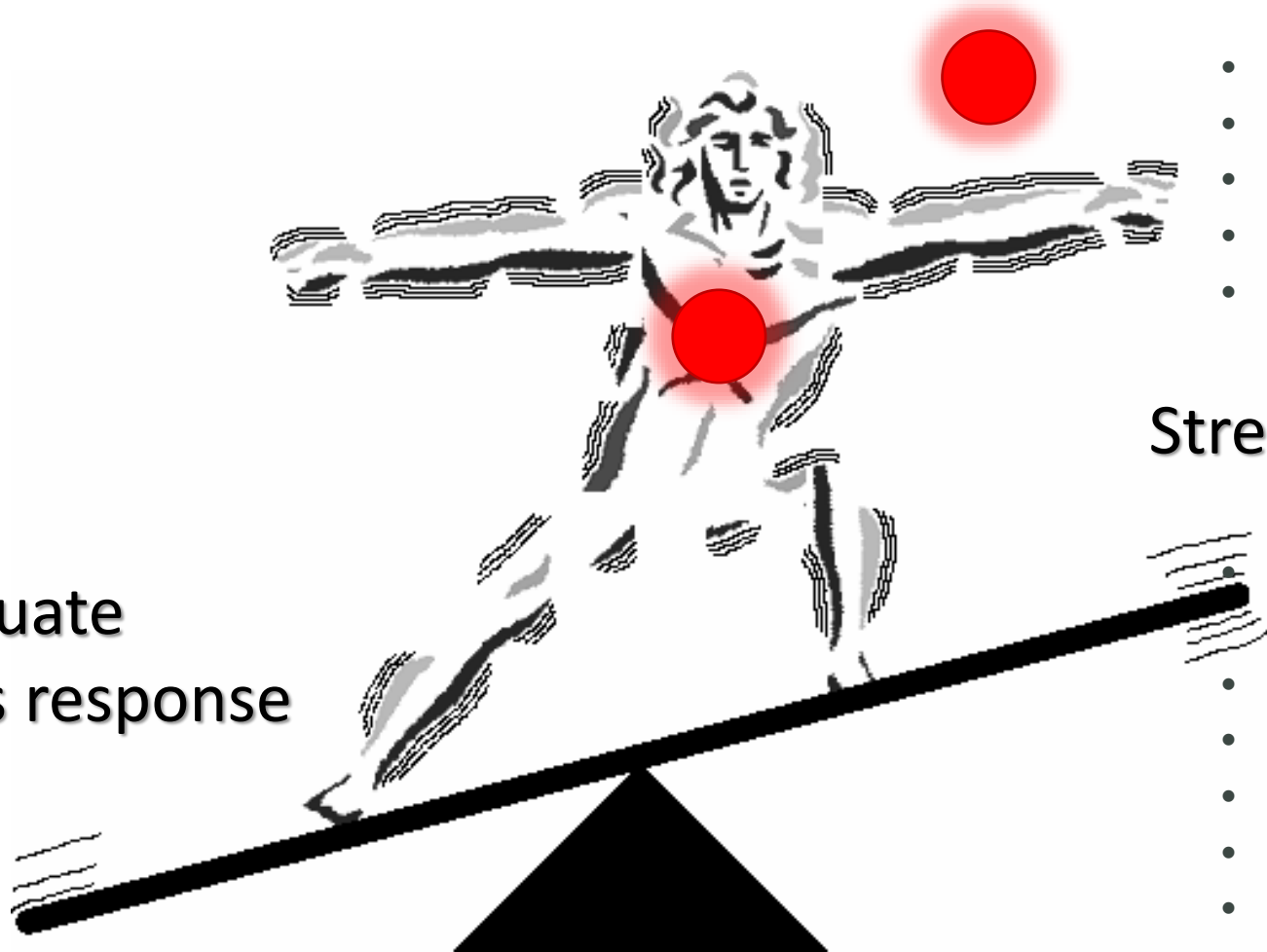
- Physical factors
- Chemical factors
- Biological factors
- Social factors
- Psychological factors

Stressors

Examples:

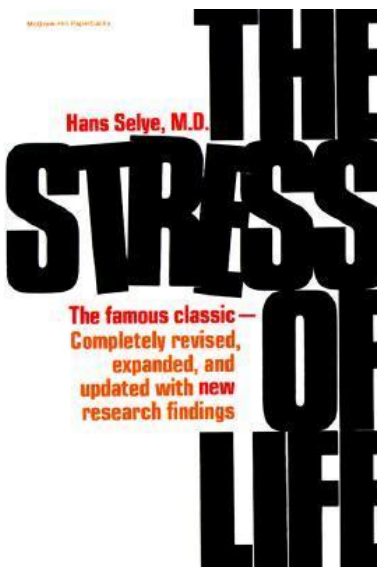
- Extreme temperature
- Physical exercise
- Toxins
- Bacteria and viruses
- Argue
- Fear.....

Adequate
stress response



Stress - definition

- “The non-specific neuroendocrine response of the body”
(Hans Selye, 1936.)
- “The non-specific response of the body to any demand for change”.
(Hans Selye, 1951.)

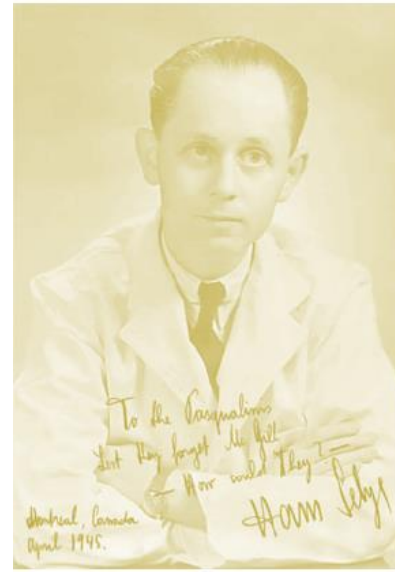


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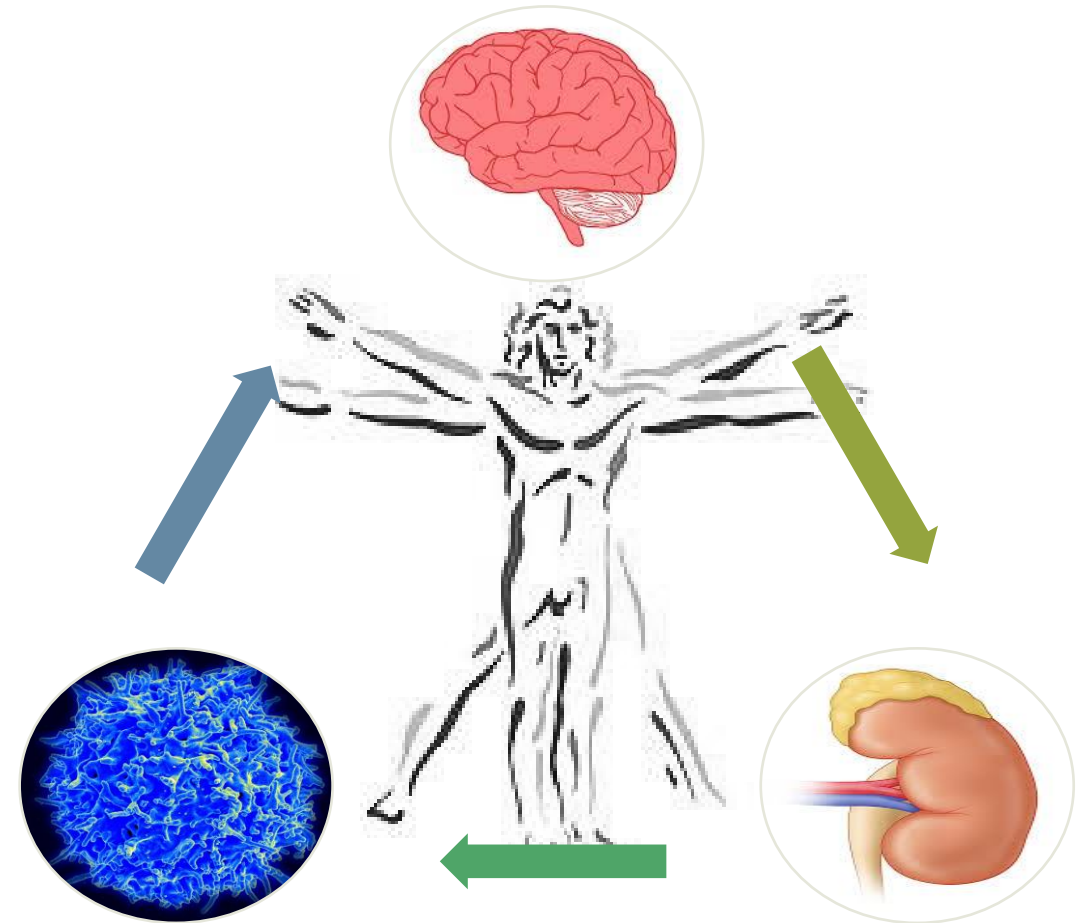
**The legacy of Hans Selye and the origins of stress research:
A retrospective 75 years after his landmark brief “Letter” to the Editor[#]
of *Nature***

SANDOR SZABO^{1,*}, YVETTE TACHE², & ARPAD SOMOGYI^{3,*}



Stress system

- Nervous system
- Endocrine system
- Immune system



Stress system

■ Hypothalamic-pituitary-adrenal axis (HPA)

CRH

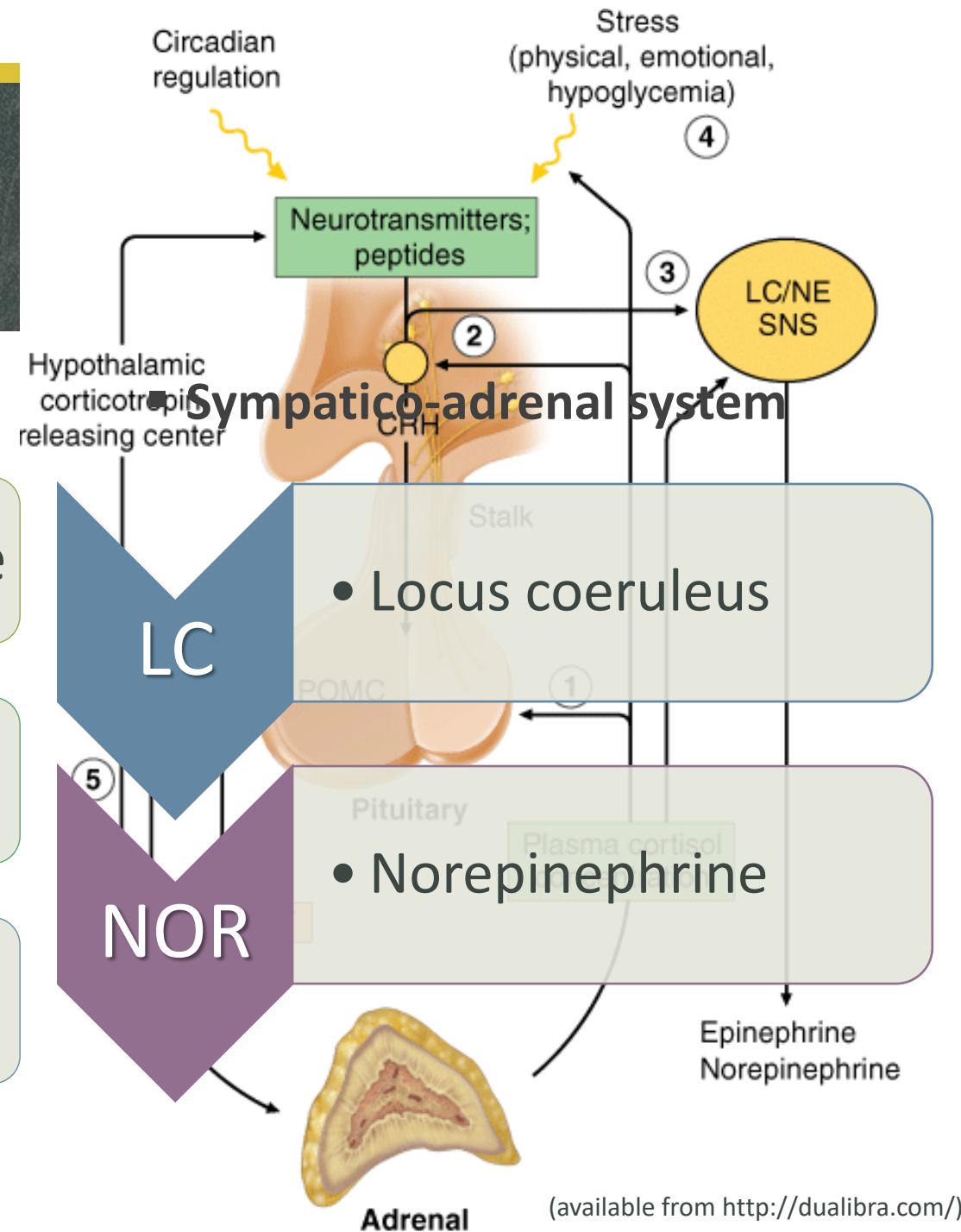
- Corticotropin-releasing hormone

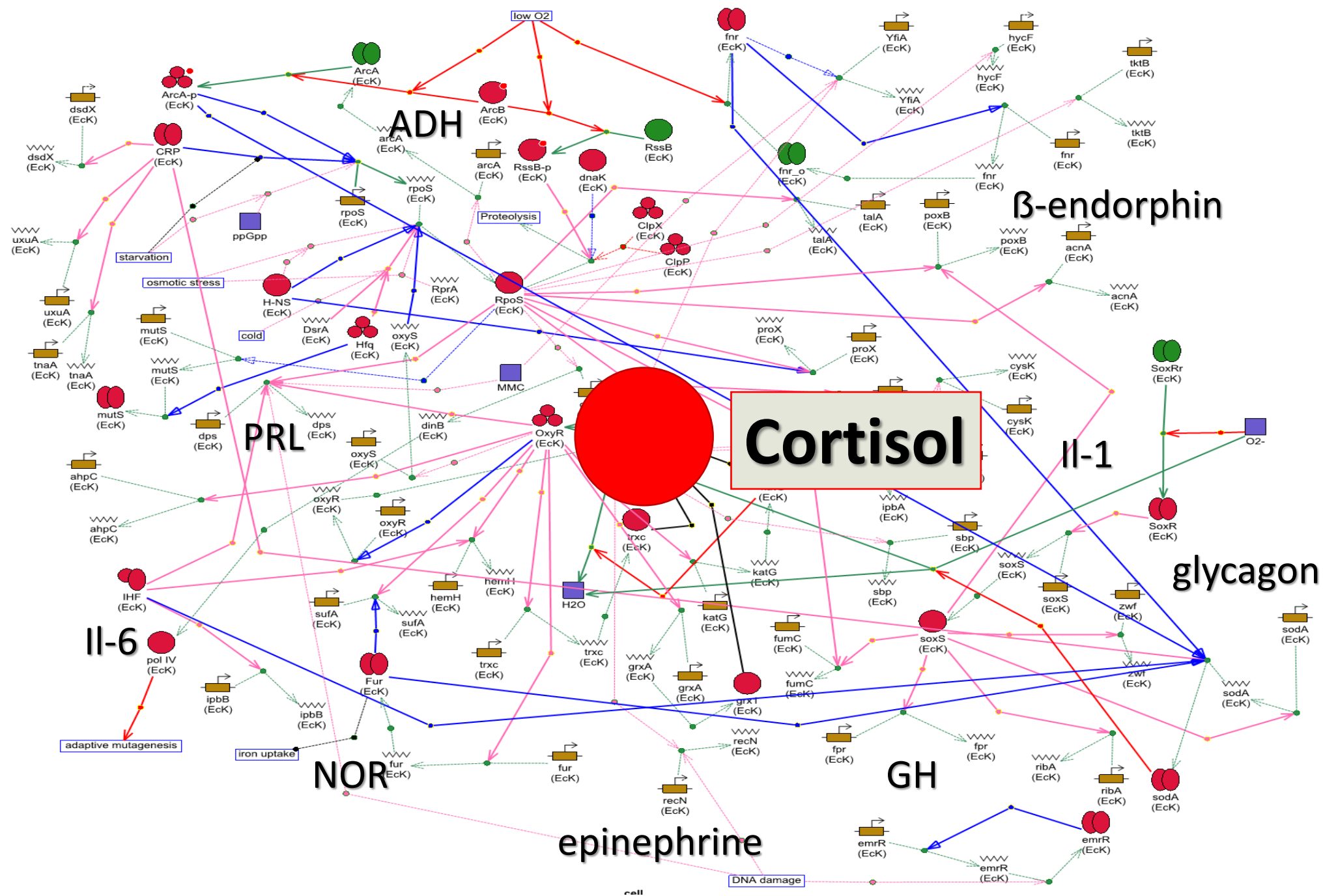
ACTH

- Adrenocorticotrophic hormone

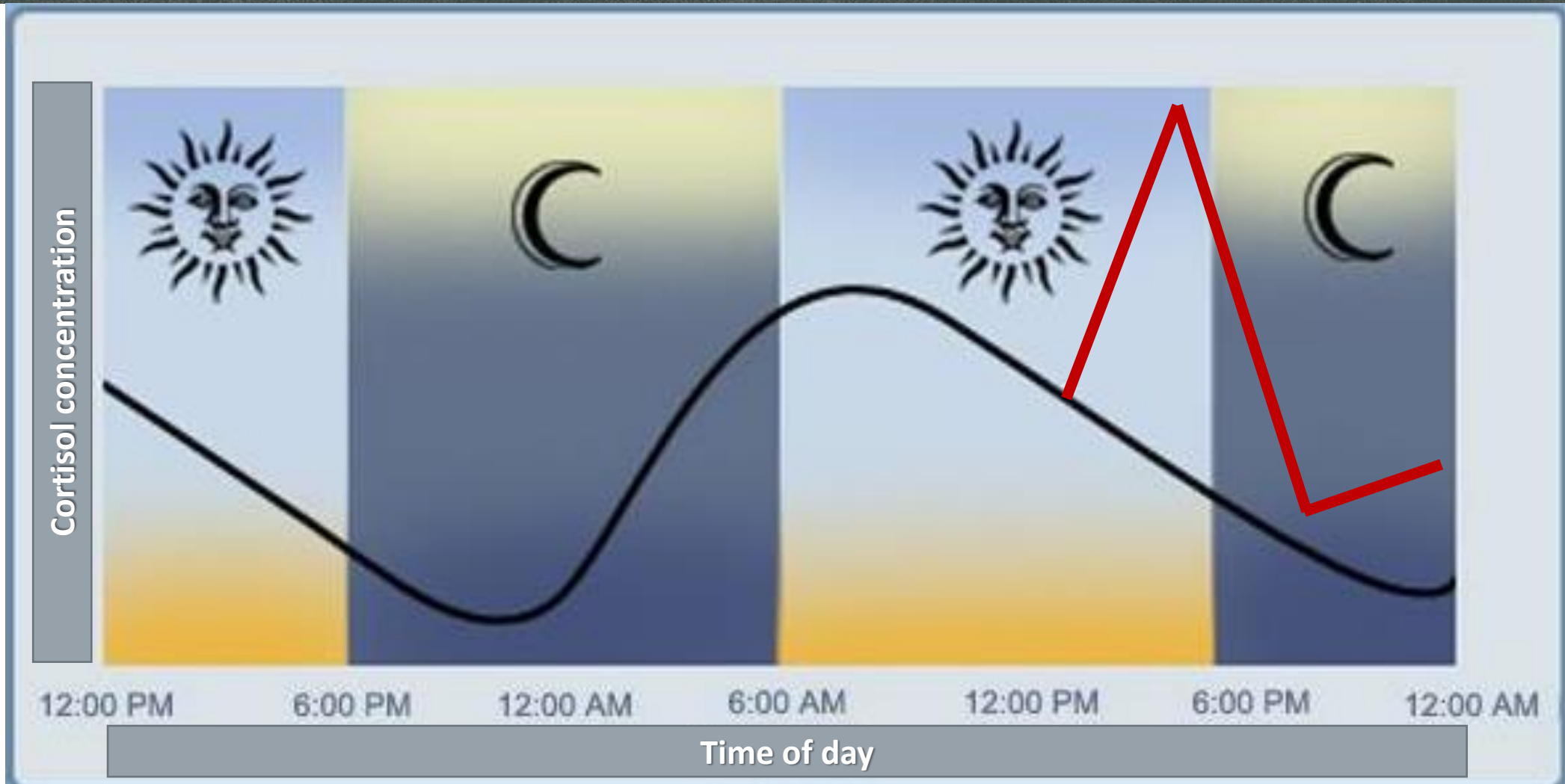
COR

- Cortisol

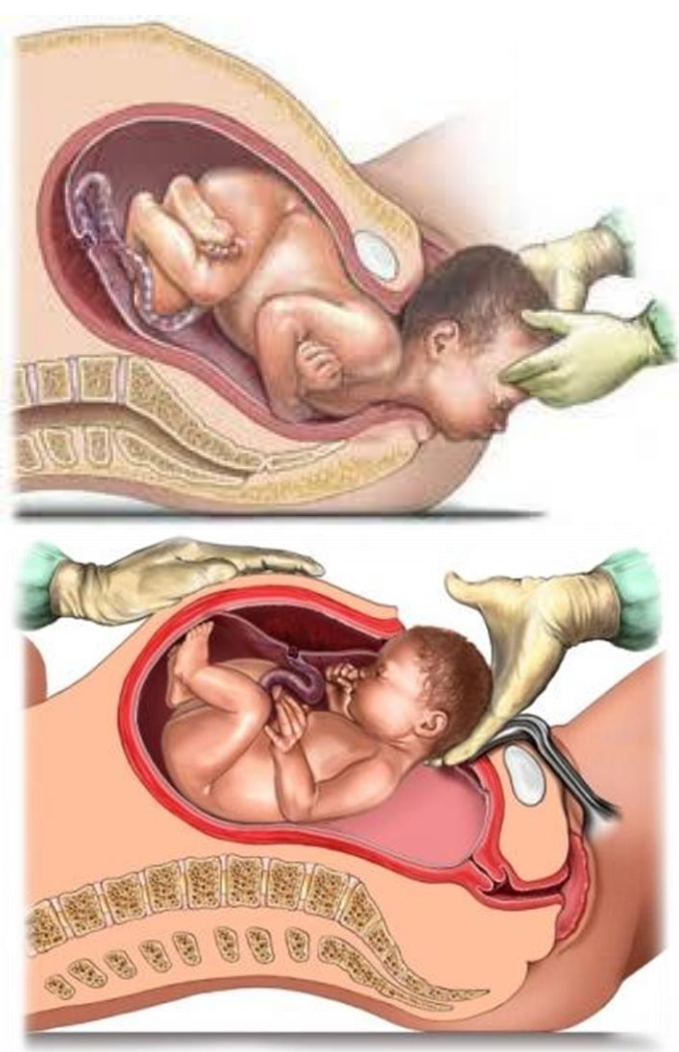




Characteristics of HPA axis function



Delivery



- Delivery methods

- Vaginal delivery
- Cesarean section

- the expulsion or extraction of a fetus and its membranes through the passageway after 20th gestational week.



The Goal

- To analyse the levels, dynamics and patterns of changes in concentrations of free salivary cortisol, total plasma cortisol and plasma ACTH in mothers whose pregnancy terminated vaginally or by caesarean section
- To determine the occurrence of ACTH-cortisol dissociation in parturients.

Material & Method

- Place of investigation:
 - Clinical Center of Vojvodina
 - Center for Laboratory Medicine
 - Department of Gynecology and Obstetrics
- Period of investigation:
 - 09th June 2014 - 24th July 2014.
- Approval obtained from Ethical Committee
- Informed Consent



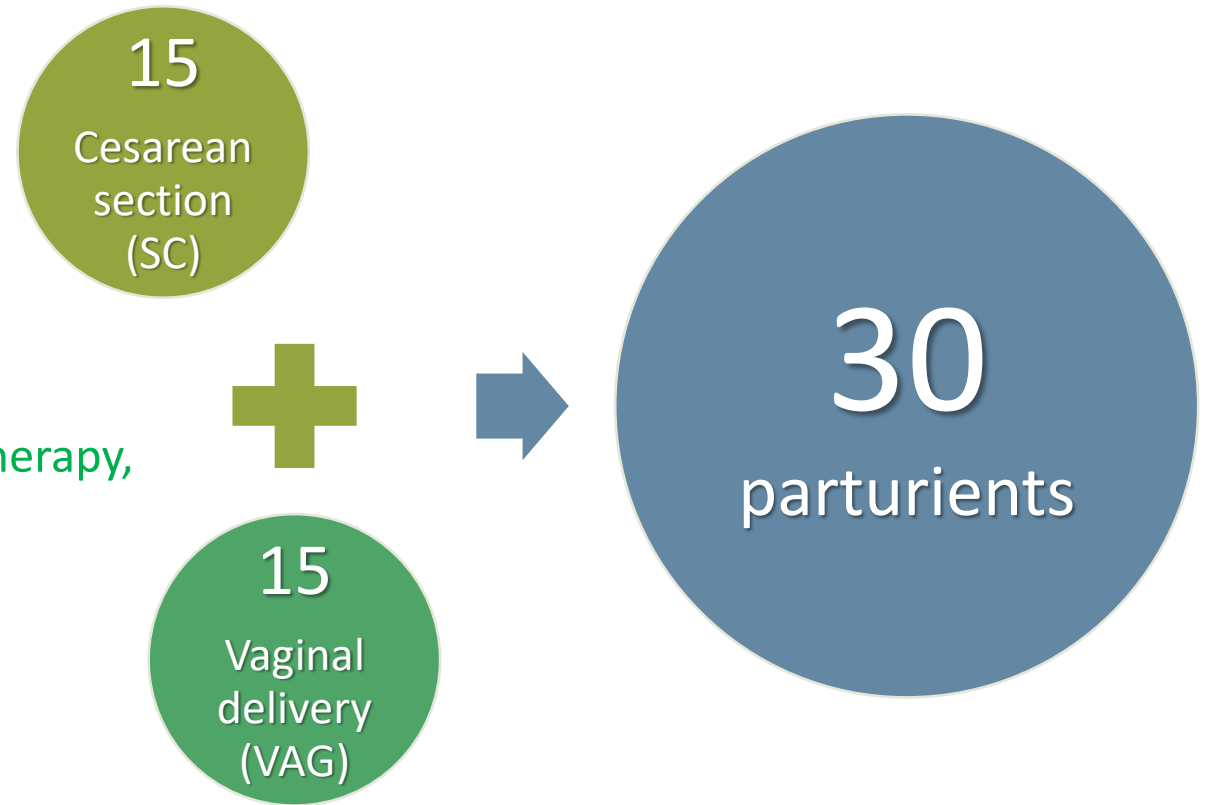
Material & Method

- **Subjects:**

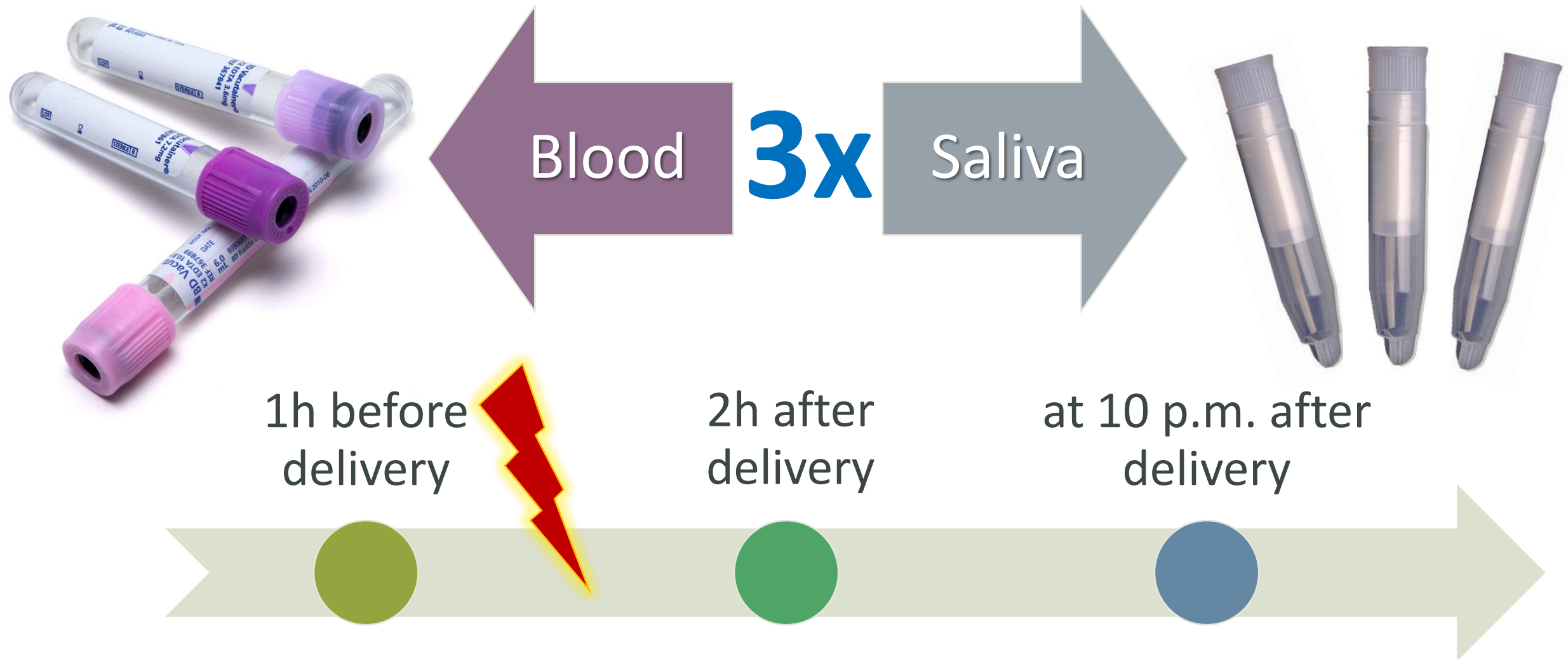
- **30 parturients**

- **Including criteria:**

- Healthy parturients , no comorbidities, no chronic therapy,
 - Regularly controlled pregnancy, normal findings
 - Singleton pregnancy,
 - Cephalic presentation,
 - 37-41 gestational age
 - Delivered vaginally or performed elective cesarean section



Material & Method - sampling

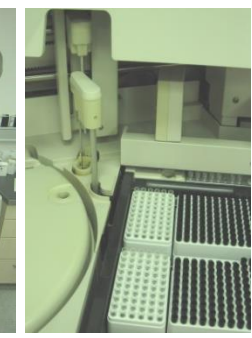


Material & Method – laboratory processing

- Blood plasma:
 - Total cortisol
 - ACTH
 - CRP
- Saliva:
 - Free cortisol



- Spin cycle
 - 3000 rpm, 3 minutes
 - 5000 rpm, 10 minutes, - 4°C
- Electrochemiluminescence method
 - Automated system- Elecsys 2010
- Immunoturbidimetric method
 - Automated system- Architect c8000



Statistical data analysis

- Descriptive statistics
- Distribution of values: *Shapiro-Wilk* test
- Significance of differences: *Student t-test* and *Mann-Whitney U* test
- Regression Analysis
- MANOVA *Repeated measures*
- *Microsoft Office – Excel*
- *SPSS 21.0 – programming language R*

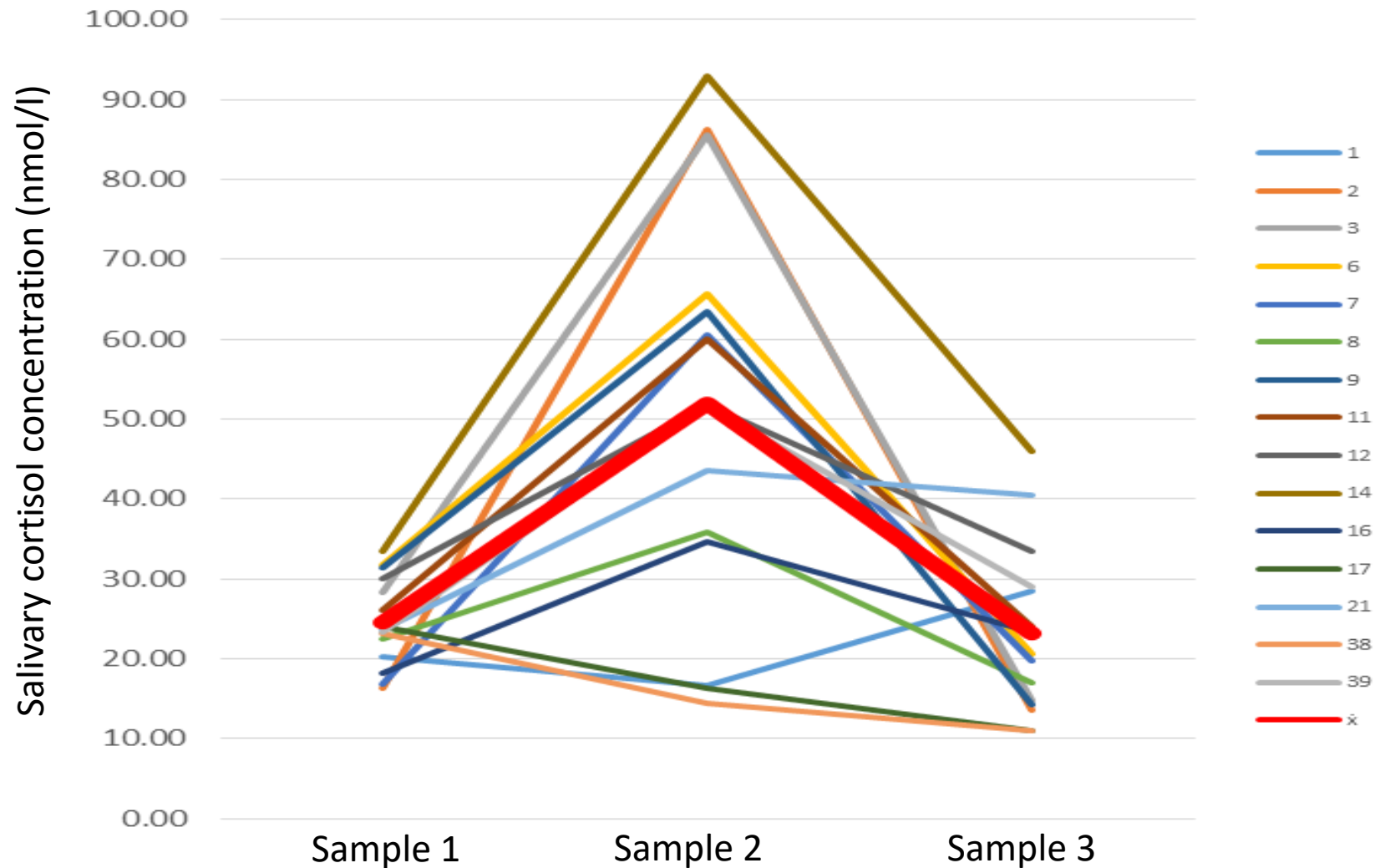


Results

Table – Basic data about parturients of both groups

	SC			VAG		
	Arithmetic mean	Minimum	Maximum	Arithmetic mean	Minimum	Maximum
Age	31	16	38	29	18	37
Body height	1.68	1.57	1.77	1.67	1.50	1.80
Body weight before pregnancy	81.19	63.5	121	77.93	58	98
Weight gain	16.97	9	27	17.60	8	28
BMI before delivery	22.70	17.72	26.15	21.76	17.36	28.96
Newborn weight	3627.33	2930	4590	3458.67	2630	4260
Newborn length	50.47	48	53	50.07	46	54
Gestational age	39.15	38	41	39.47	38	41
Number of deliveries	1.73	1	3	1.47	1	4
p > 0,05	BMI – body mass index	SC- first group	VAG- second group			

Results– variability of individual values

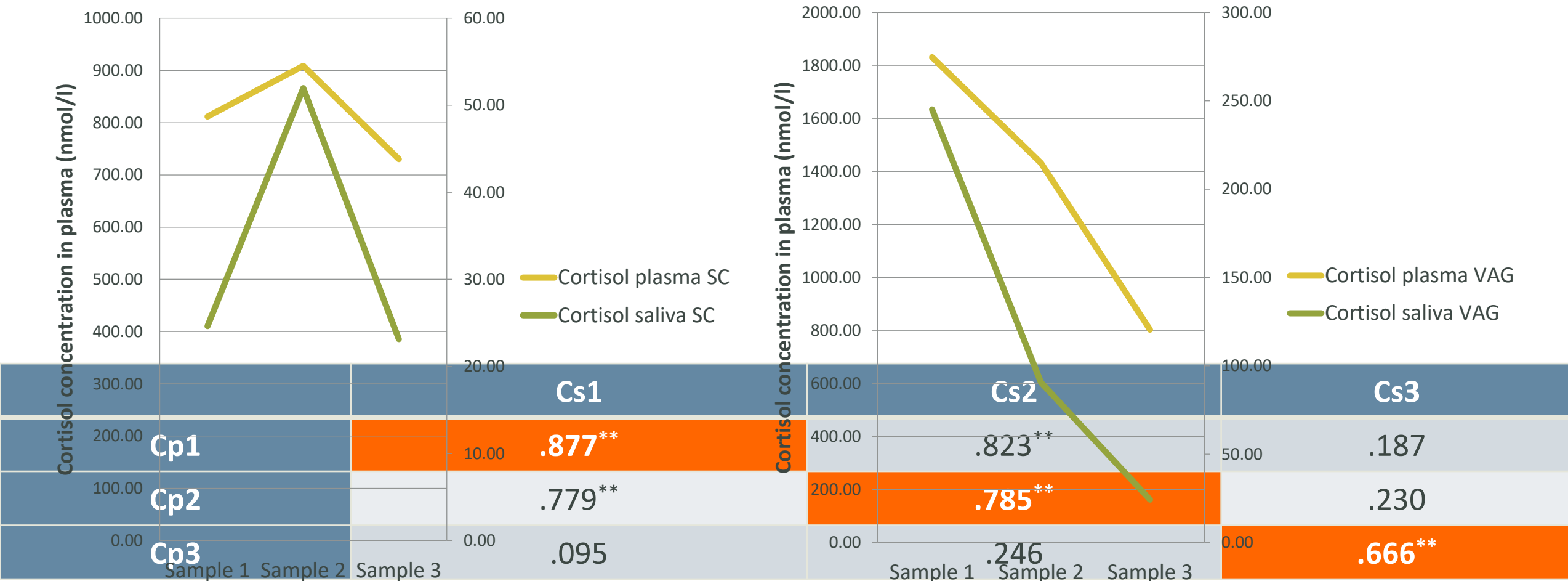


Analysis of levels, dynamics and secretion pattern of hormone

Table - Descriptive analysis of plasma cortisol (nmol/l) levels by samples and groups

SC									
	N	AS	SD	Mediana	Minimum	Maximum	Varians	Curtosis	Skewness
Cp1	15	811.88	182.08	781.70	559.20	1218.00	33153.30	.31	.74
Cp2	15	908.77	237.59	882.90	553.90	1377.00	56448.00	-.57	.33
Cp3	15	730.07	259.74	725.50	235.40	1049.00	67466.56	-.90	-.46
VAG									
	N	AS	SD	Mediana	Minimum	Maximum	Varians	Curtosis	Skewness
Cp1	15	1831.27	765.17	1652.00	1130.00	3952.00	585483.35	3.76	1.94
Cp2	15	1431.58	362.37	1429.00	952.70	2285.00	131311.77	1.78	1.32
Cp3	15	803.25	207.73	844.80	382.80	1123.00	43152.91	-0.36	-0.43
Cp- plasma cortisol in certain measurement N- number of samples, AS- arithmetic mean, SD- standard deviation									

Graph – Changes of salivary and plasma cortisol concentrations in SC group (left) and VAG group (right)



Results— cortisol in saliva and blood plasma

Table - Comparison of salivary cortisol levels between groups by samples and relative changes

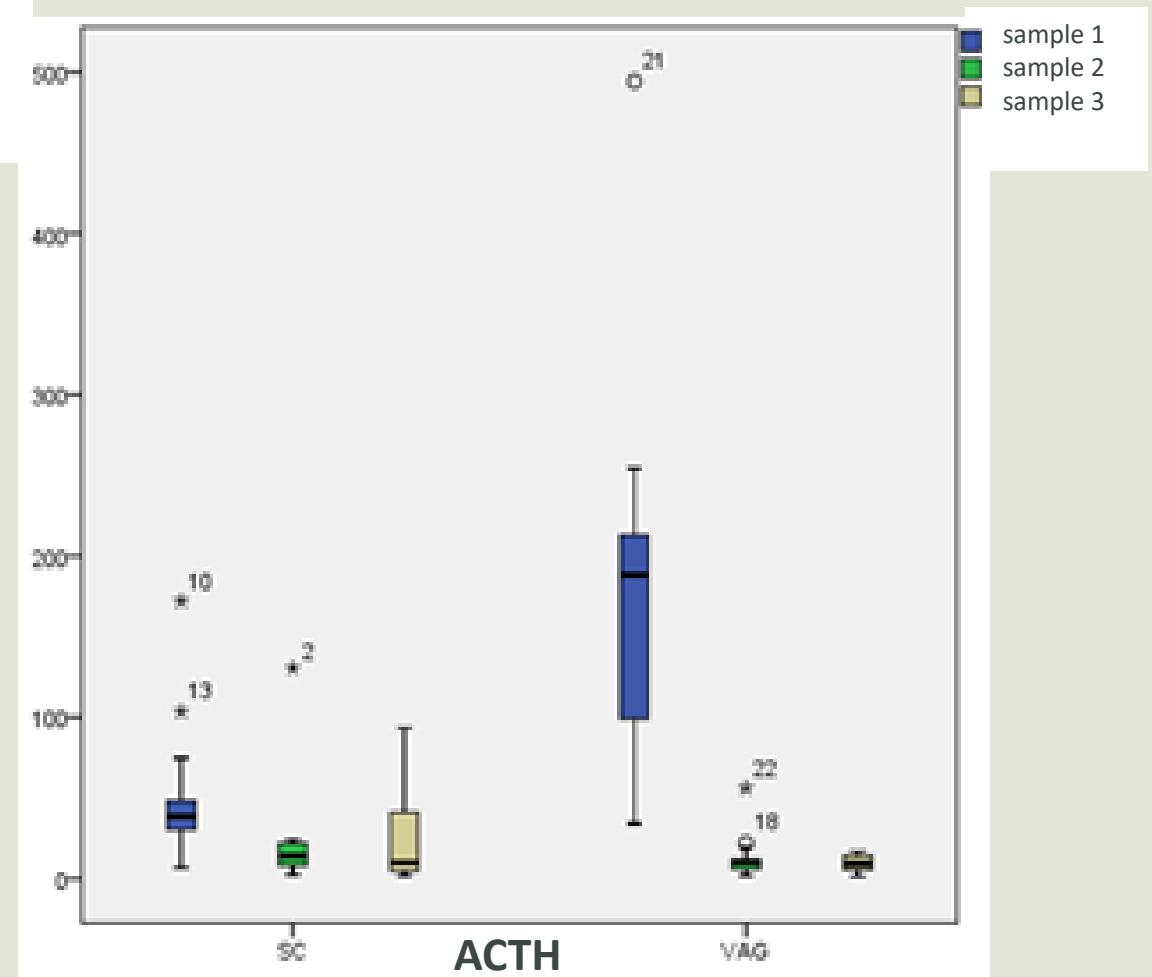
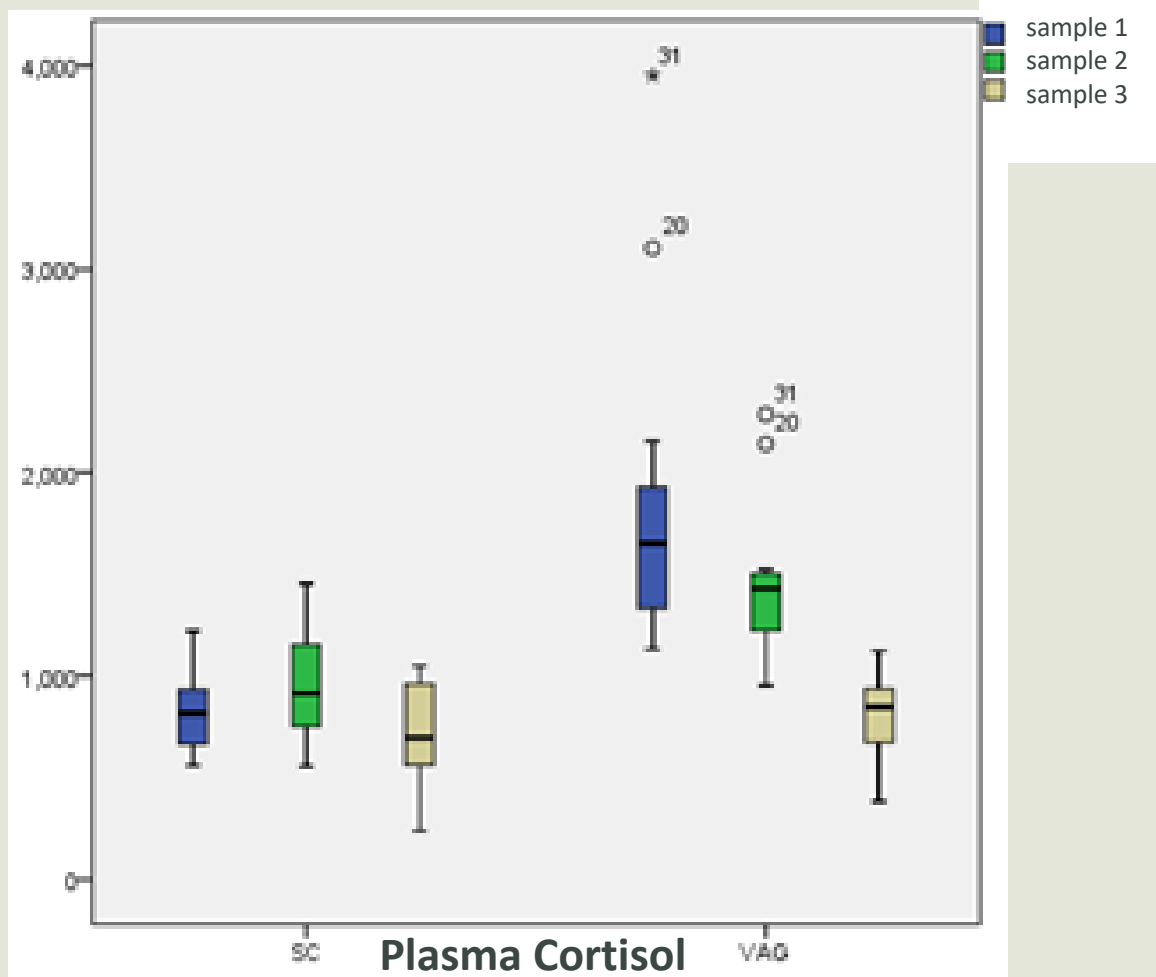
	Sample 1	Sample 2	Sample 3	Sample 2/1	Sample 3/1
$\bar{x}$ (SC)	24.64	51.96	23.14	2.16	0.96
$\bar{x}$ (VAG)	245.20	90.58	24.25	0.58	0.23
p	0.02*	0.12	0.77	4.02E-05**	5.85E-07**

Table - Comparison of plasma cortisol levels between groups by samples and relative changes

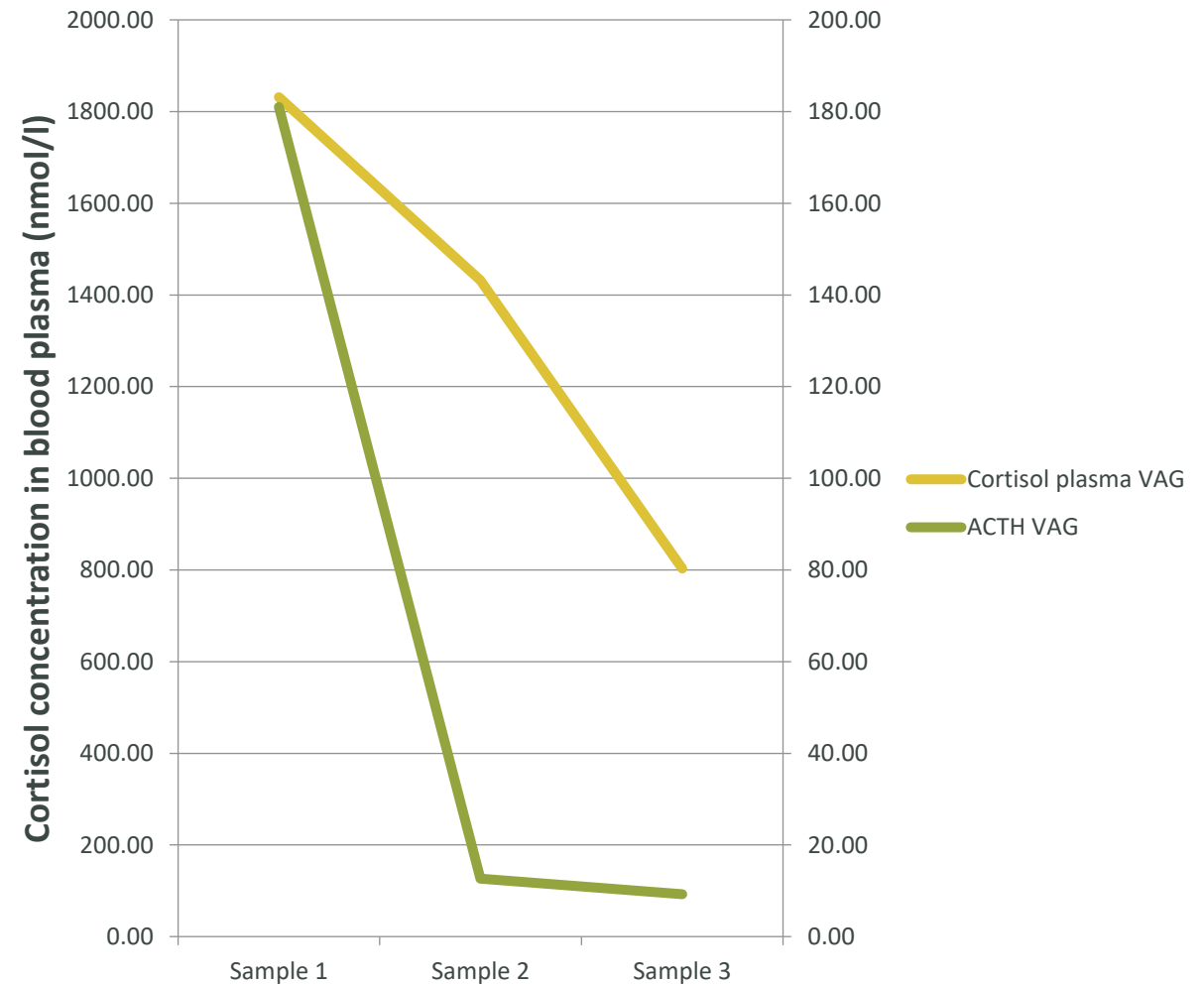
	Sample 1	Sample 2	Sample 3	Sample 2/1	Sample 3/1
$\bar{x}$ (SC)	811.88	908.77	730.08	1.14	0.94
$\bar{x}$ (VAG)	1831.27	1431.58	803.25	0.83	0.48
P	2.63E-05**	6.78E-05**	0.40	0.001**	0.0002**

*p< 0,05; **p<0,01; $\bar{x}$ -arithmetic mean concentration of certain sample

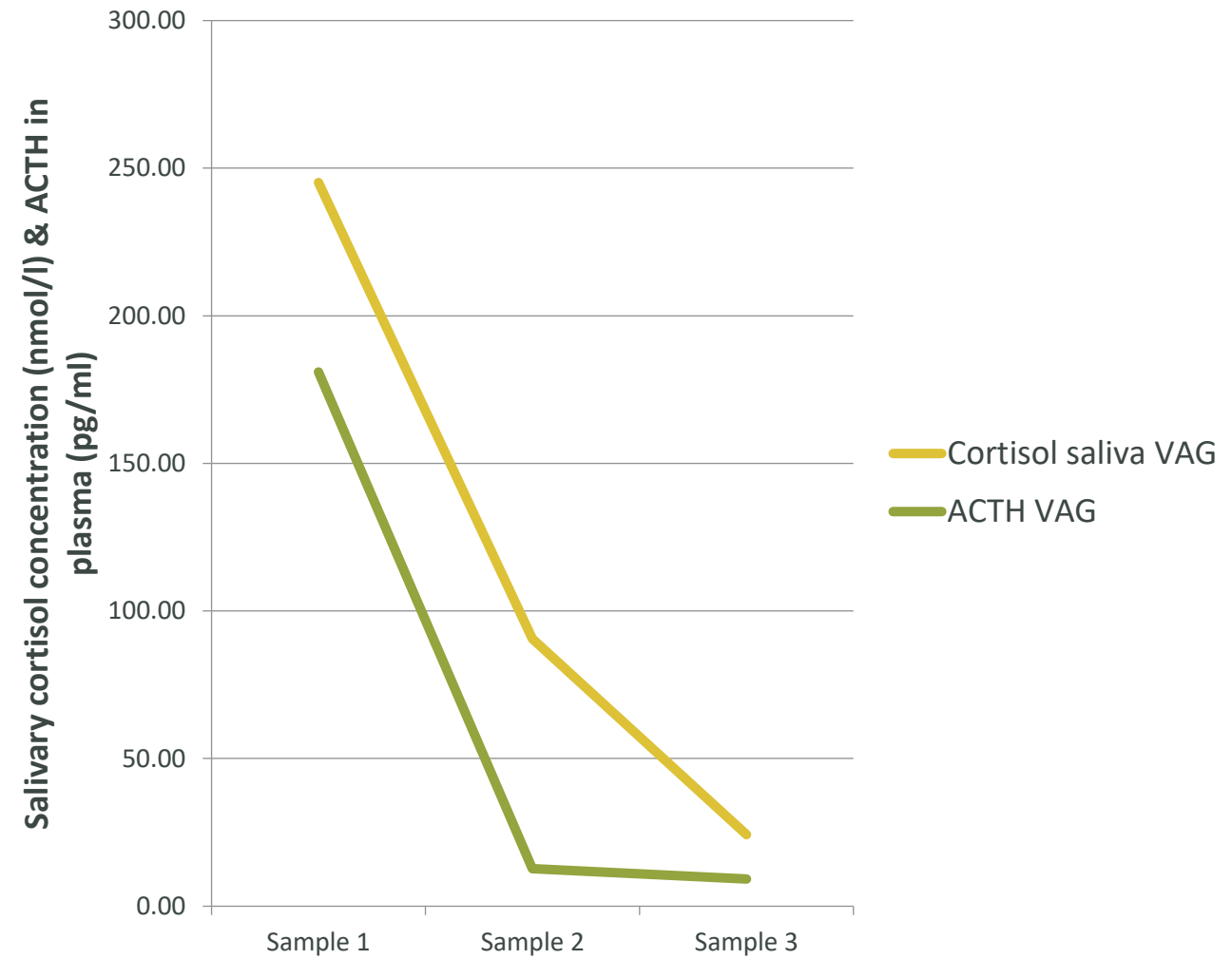
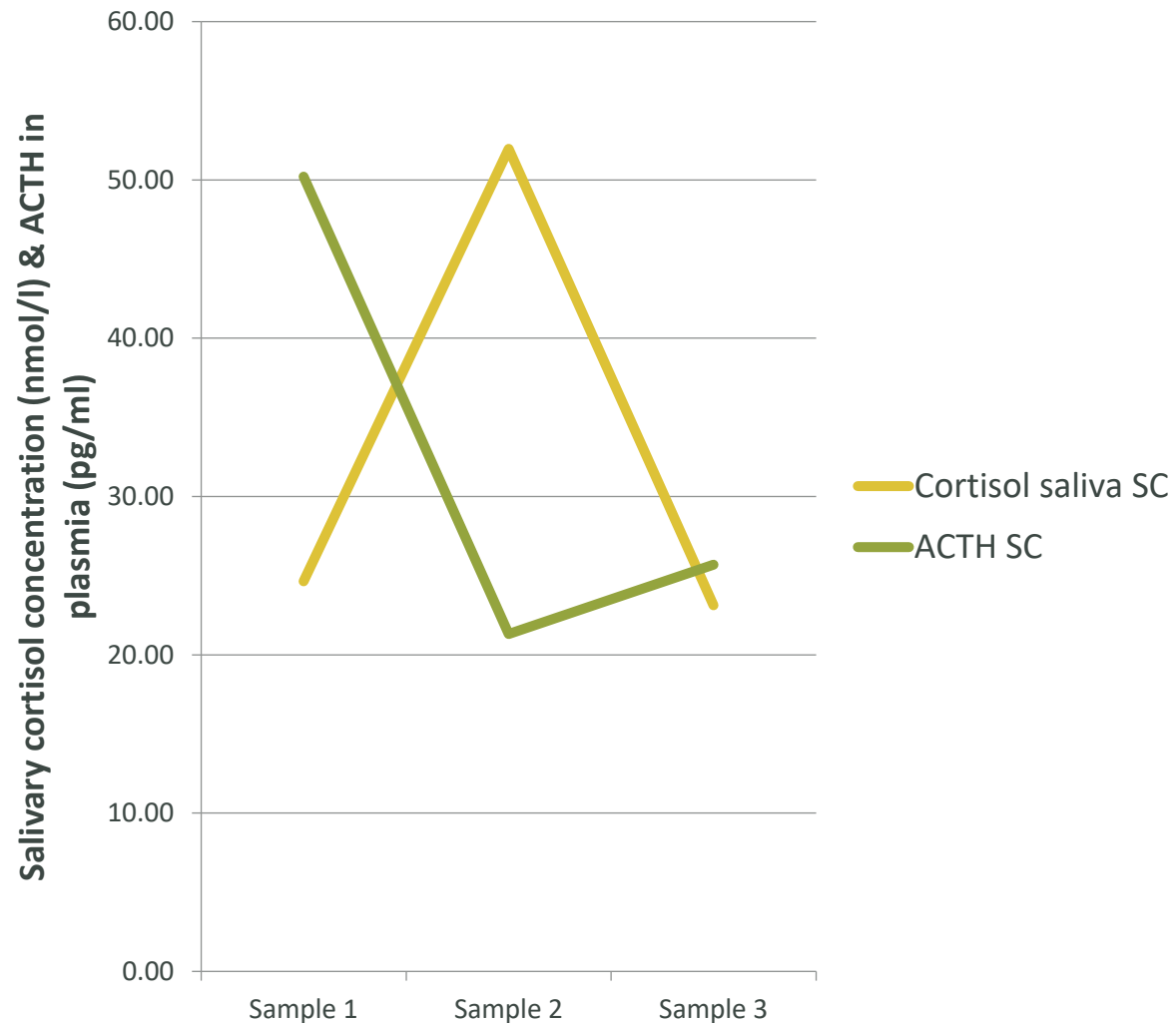
Distribution of values



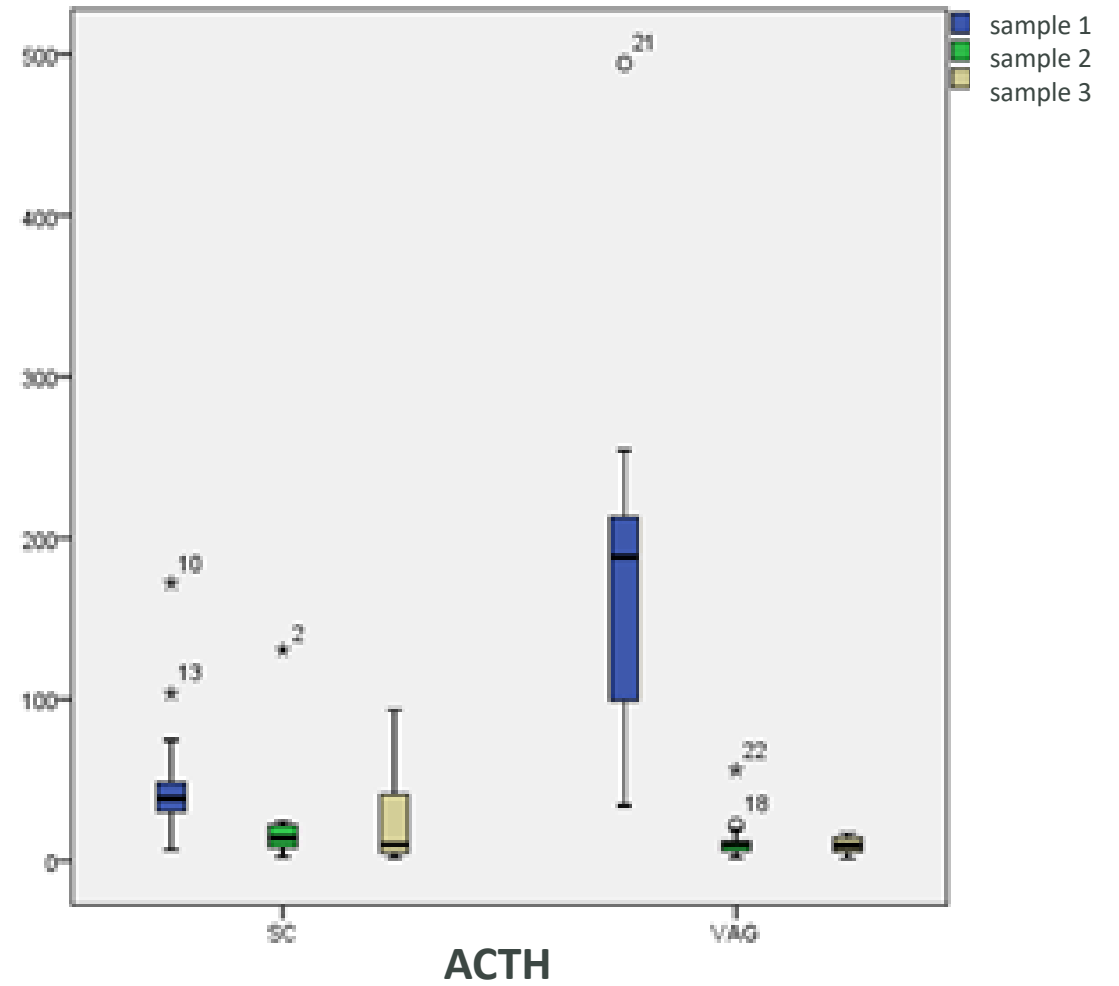
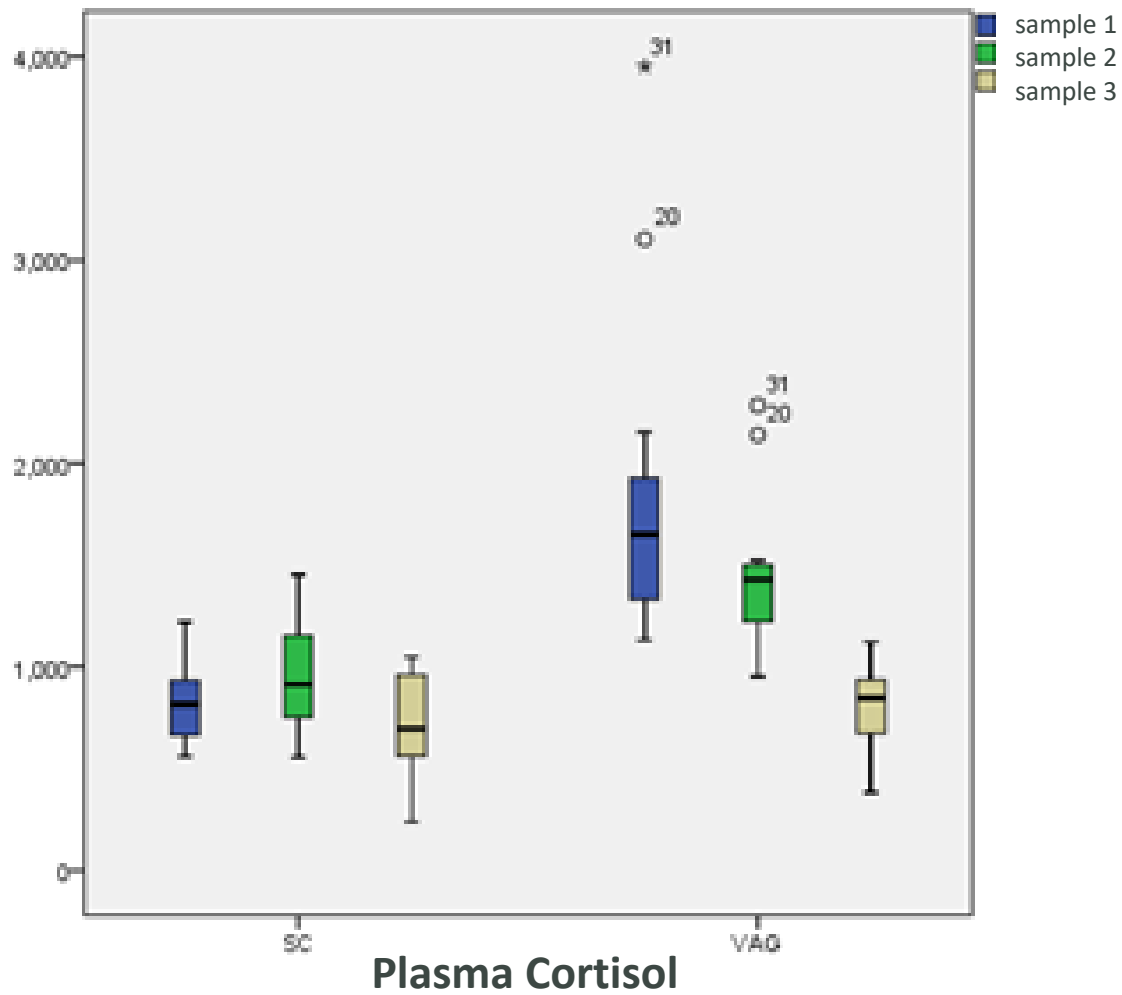
Graph- Secretion patterns of plasma cortisol and ACTH in SC group (left) and VAG group (right)



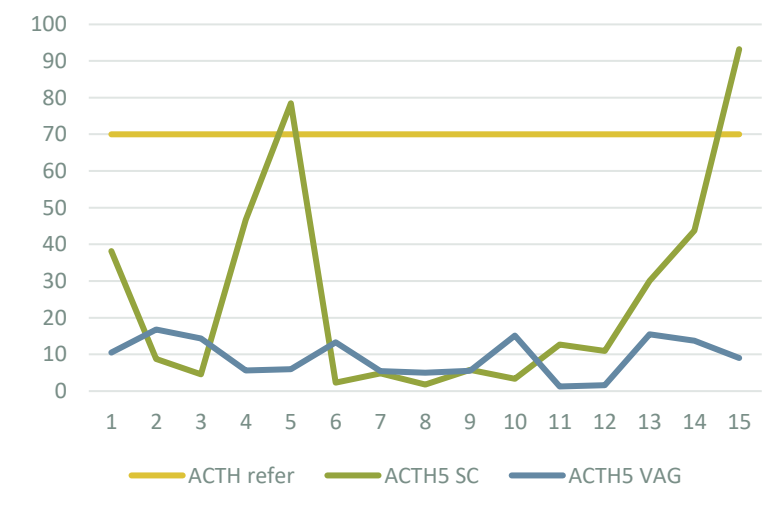
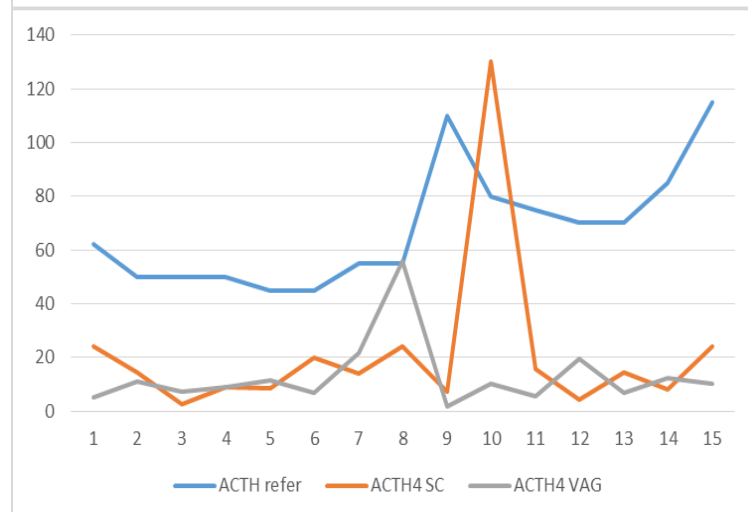
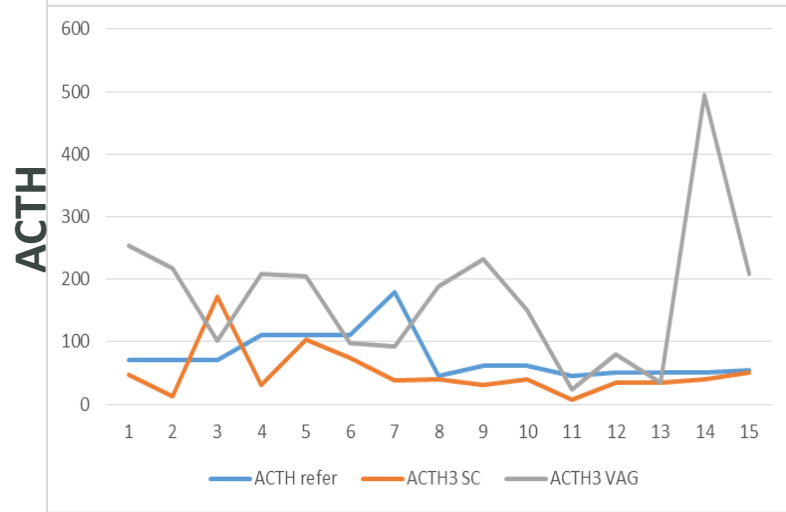
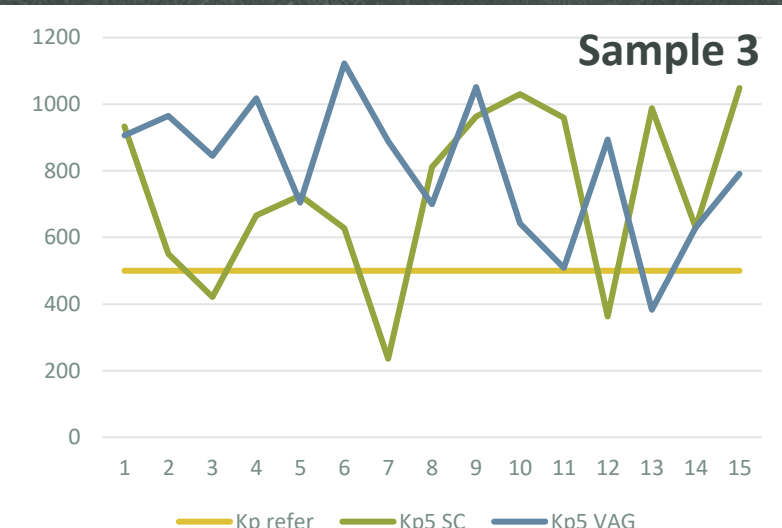
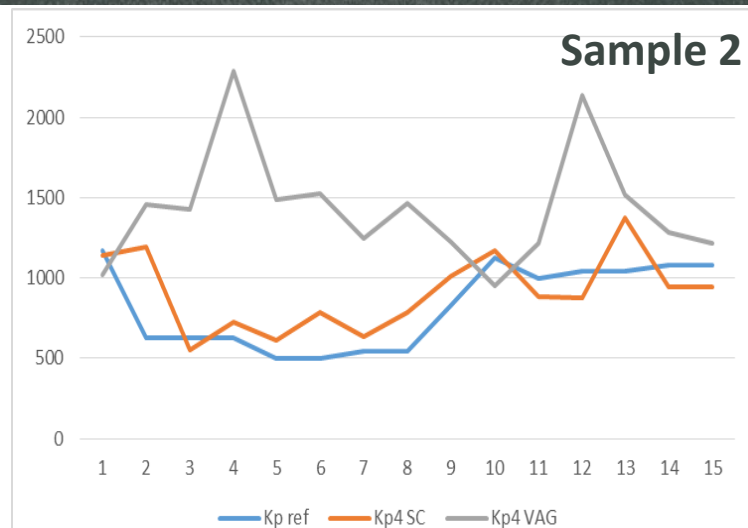
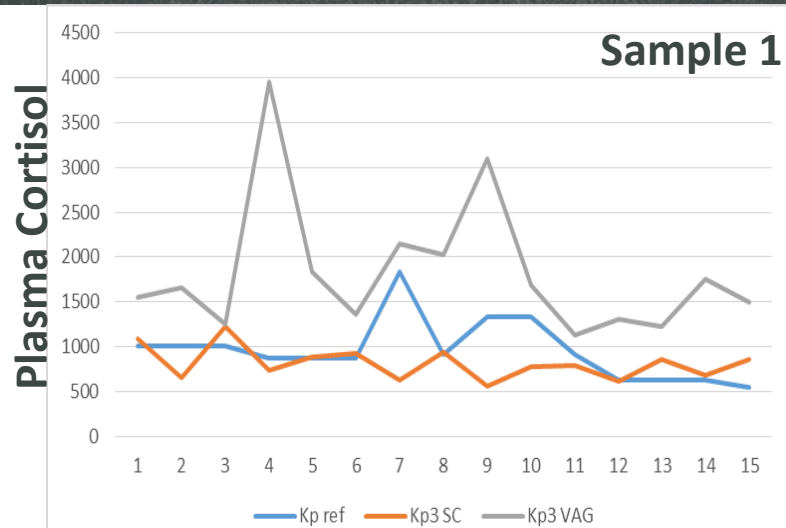
Graph- Secretion patterns of salivary cortisol and ACTH in SC group (left) and VAG group (right)



Distribution of values



Analysis depending on the time of day



	SC						VAG					
Referentna grupa	Kp1	Kp2	Kp3	ACTH1	ACTH2	ACTH3	Kp1	Kp2	Kp3	ACTH1	ACTH2	ACTH3
K1	x						↑↑					
K2		x						↑↑				
K3			↑↑						↑↑			
ACTH1				x						↑		
ACTH2					↓↓						↓↓	
ACTH3						↓↓						↓↓

Conclusions

- **Conclusions:** The results of this study indicate the differences in the secretion pattern of ACTH and cortisol depending on delivery method.
- Vaginal delivery causes intense and relatively short-lived response of the neuroendocrine system- levels of ACTH and cortisol showed a decreasing trend with a significant degree of mutual influence.
- In women delivered by caesarean section is observed the ACTH-cortisol dissociation in terms of decline of ACTH concentrations accompanied by an increase in cortisol levels during delivery.
- This indicates the presence of ACTH-independent factors affecting the adrenocortical activity level. The true nature of this phenomenon cannot be clarified by the applied research methodology.



In memoriam

Egon Diczfalussy



Thank You, professor!