



# CLORMADINONE ACETATO: I BENEFICI NON CONTRACCETTIVI

*Lodi, 28 Marzo 2009*

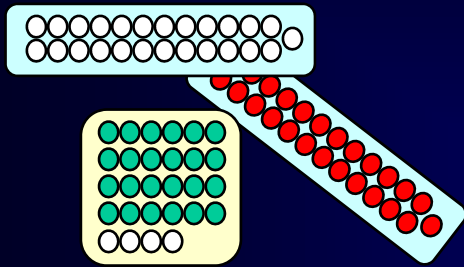
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Fondazione Maugeri, Università di Pavia

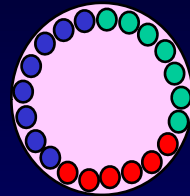
# BENEFICI NON CONTRACCETTIVI DELLA CONTRACCEZIONE ORMONALE (1)



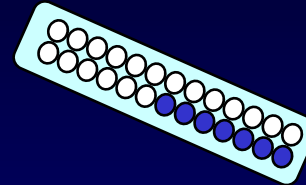
# HORMONAL CONTRACEPTIVE OPTIONS



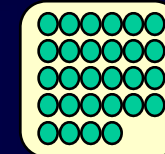
*Monophasic  
Estro-Progestin*



*Triphasic  
Estro-Progestin*



*Biphasic  
Estro-Progestin*



*Monophasic  
Progestin*

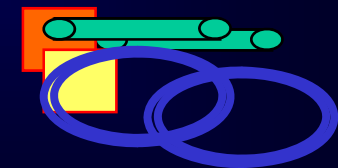
## **REDUCTION OF ESTROGEN DOSE**

- > 30 mcg EE
- 30 mcg EE
- 20 mcg EE
- 15 mcg EE

## **DEVELOPMENT OF NEW PROGESTINS**

- type
- dose

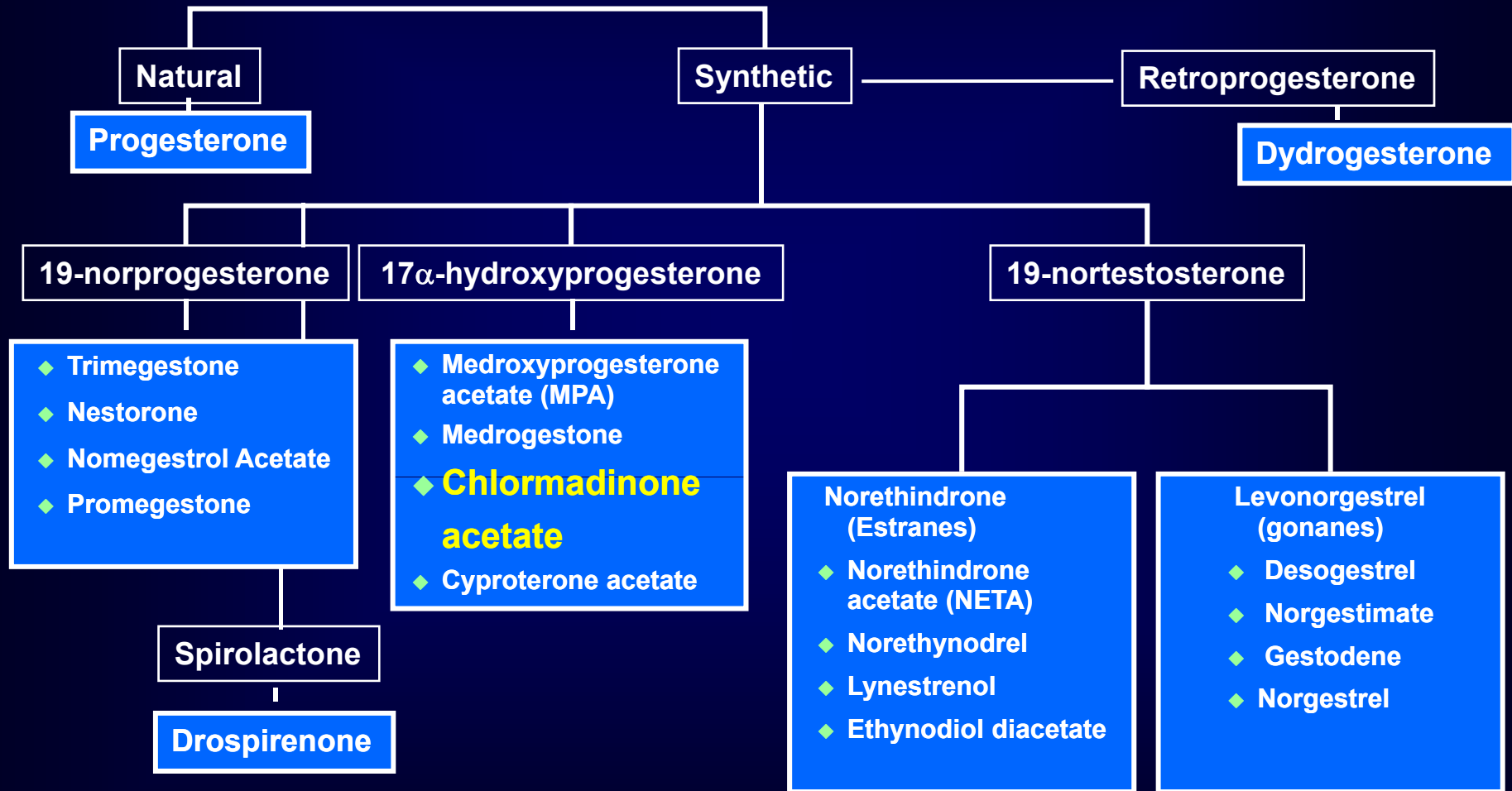
*New Options*



# BENEFICI NON CONTRACCETTIVI DELLA CONTRACCZIONE ORMONALE (2)



# Progestogens



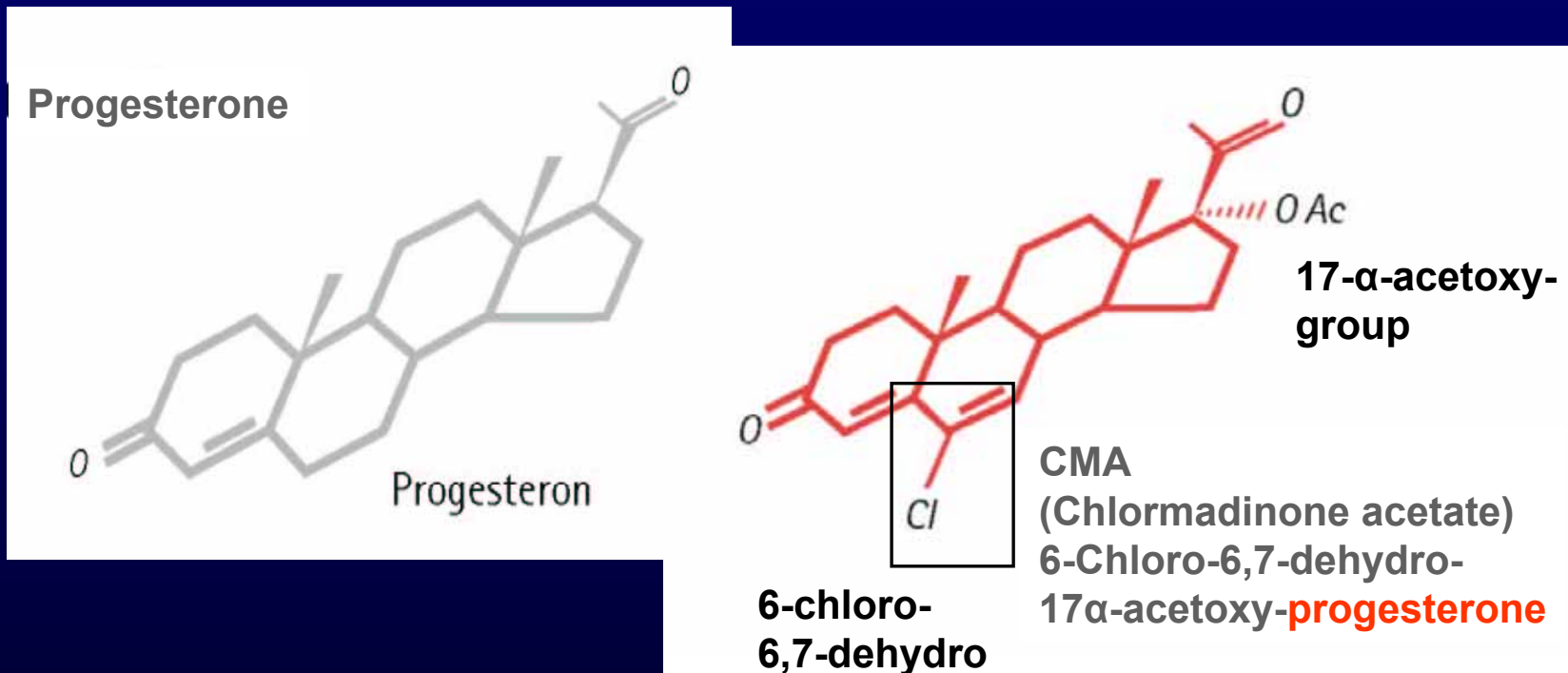
*Courtesy of Nicola Pluchino, 2009*

# EFFETTI DEI PROGESTINICI

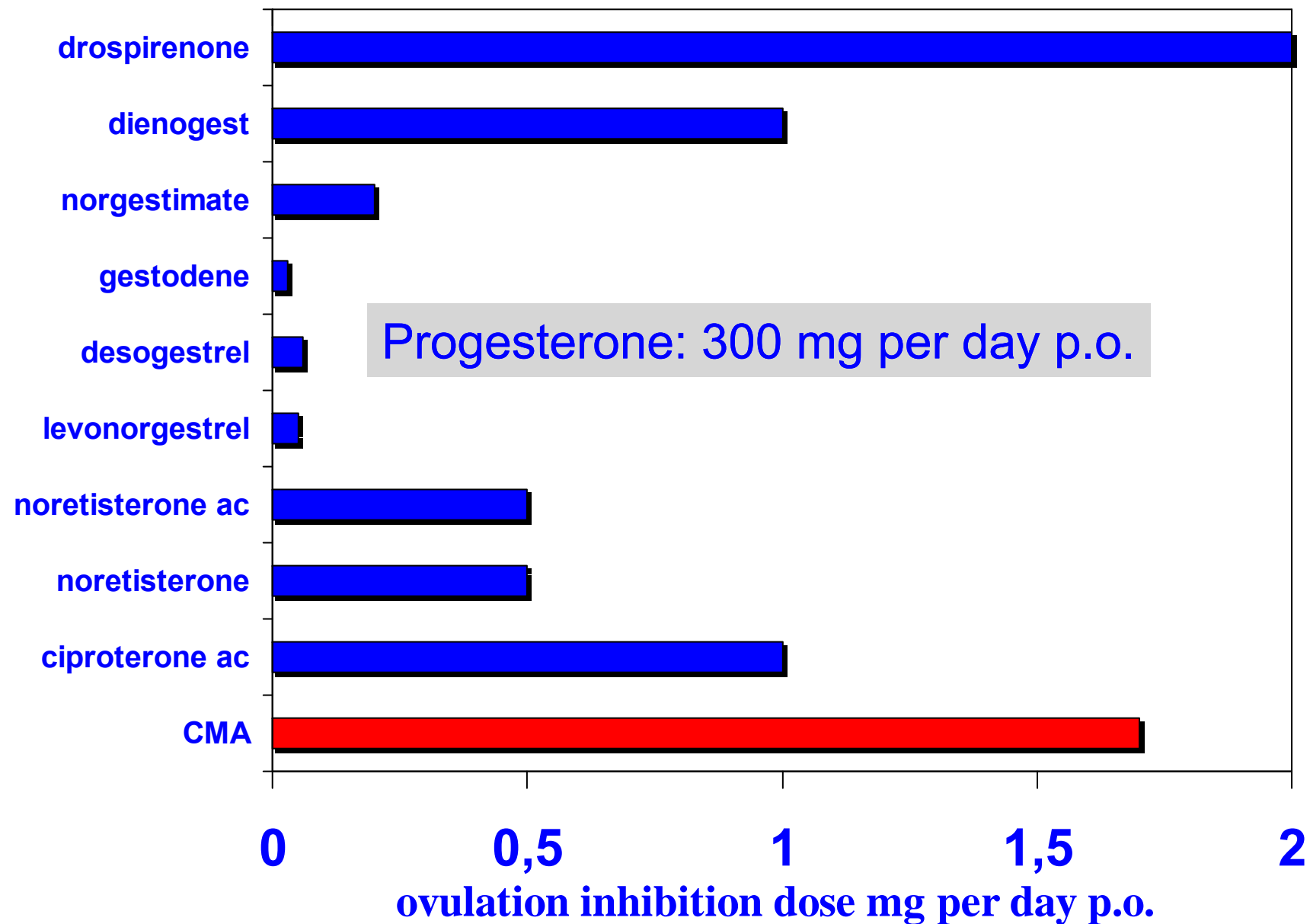
	Trasforma- zione endometriale	Effetto estroge- nico	Effetto anti- estrogenico	Effetto androge- nico	Effetto anti-andro- genico	Effetto gluco- corticoide	Effetto anti-mineral- corticoide
<b>Progesterone</b>	+	-	+	-	(+)	(+)	+
<b>Clormadinone ac</b>	+	-	+	-	+	(+)	-
Ciproterone ac.	+	-	+	-	+	+	-
Dienogest	+	-	+	-	+	-	-
Desogestrel	+	-	+	+	-	-	-
Drospirenone	+	-	+	-	+	-	+
Norgestimate	+	-	+	+	-		
Gestodene	+	-	+	+	-		+
Levonorgestrel	+	-	+	+	-	-	-
Noretisterone	+	(+)	+	+	-	-	-

*modificata da Kuhl & Jung-Hoffmann, 1999*

# STRUTTURA DEL CMA & DEL PROGESTERONE

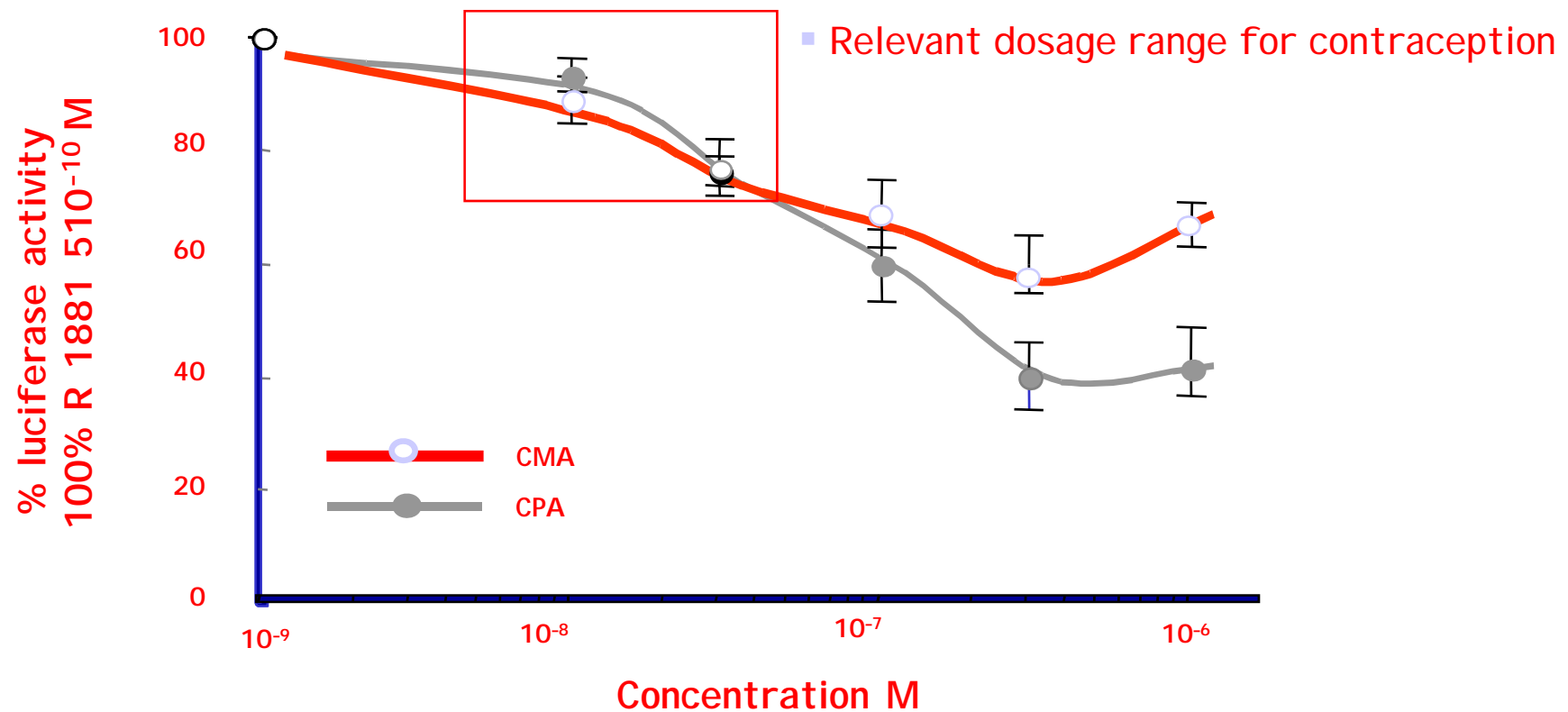


# DOSE DI CMA & INIBIZIONE OVULAZIONE

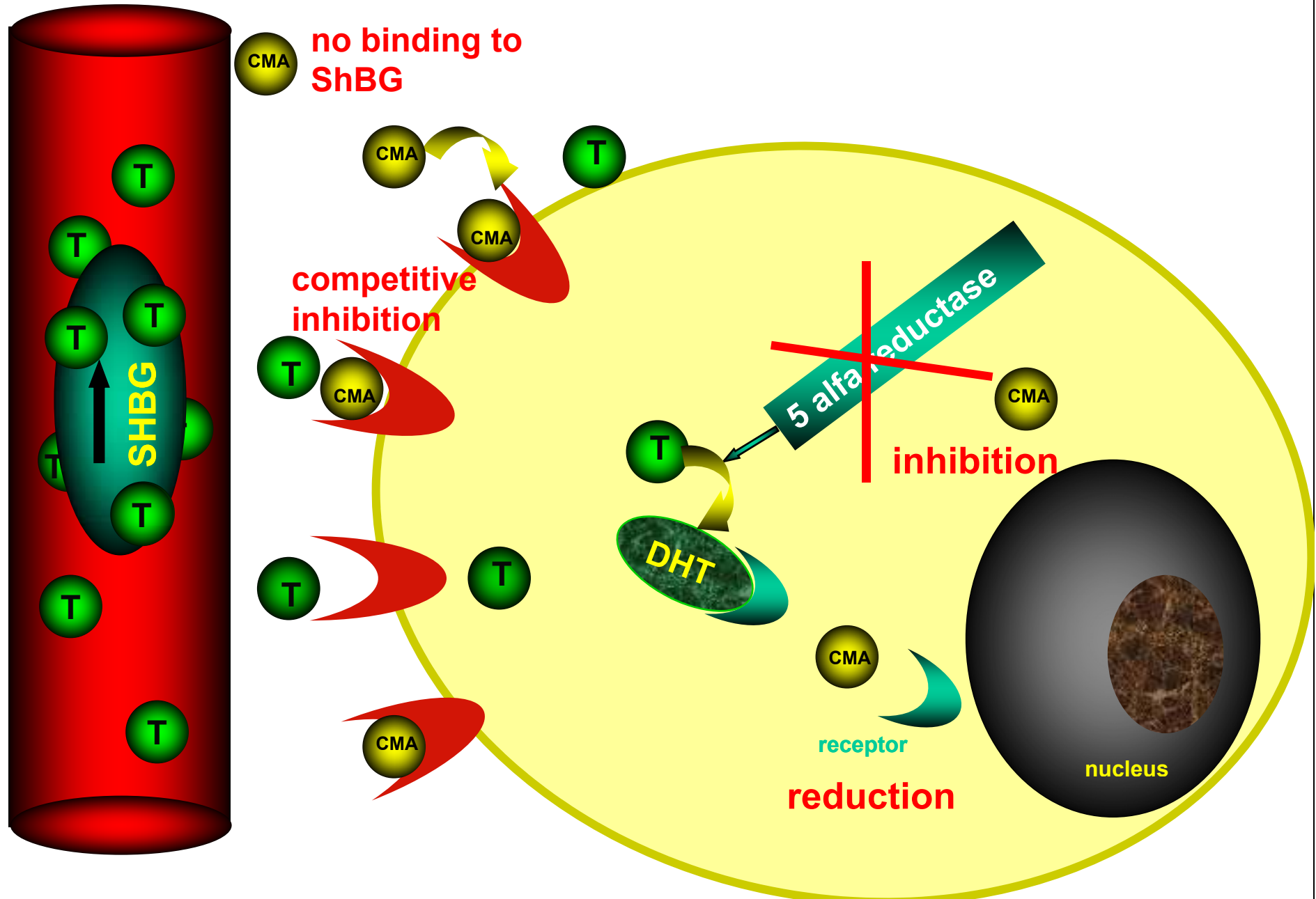


# CMA & ATTIVITA' ANTIANDROGENICA

Antiandrogenic activity of chlormadinone acetate (CMA)  
vs. cyproterone acetate (CPA)



# CMA/EE & PROPRIETA' ANTIANDROGENICHE



## CMA & NEUTRALITA' METABOLICA

- *Studio in aperto in 21 pazienti con alto rischio vascolare e trattate con CMA 5mgx2/die dal gg 6-8 al 25 del ciclo*

Livelli plasmatici	basale	12 mesi	30 mesi
Glucosio (g/l)	0.83 ± 0.05	0.83 ± 0.08	0.80 ± 0.06
Trigliceridi (g/l)	0.70 ± 0.18	0.61 ± 0.15	0.58 ± 0.22
Colesterolo (g/l)	2.02 ± 0.47	1.89 ± 0.47	2.08 ± 0.33
HDL-C (g/l)	0.42 ± 0.06	0.46 ± 0.09	0.40 ± 0.06
LDL-C (g/l)	1.46 ± 0.30	1.30 ± 0.46	1.54 ± 0.46
Apoprot. B (g/l)	1.07 ± 0.21	0.99 ± 0.27	1.16 ± 0.39
Apoprot. A1 (g/l)	1.48 ± 0.16	1.4 ± 0.19	1.44 ± 0.13
Antitromb. III (%)	101.4 ± 6.8	108.23 ± 7.6	102.5 ± 10.1
Insulina (µl/ml)	15.5 ± 2	15.5 ± 2	14 ± 3

**Il trattamento a lungo termine con CMA non comporta variazioni significative dei parametri metabolici**

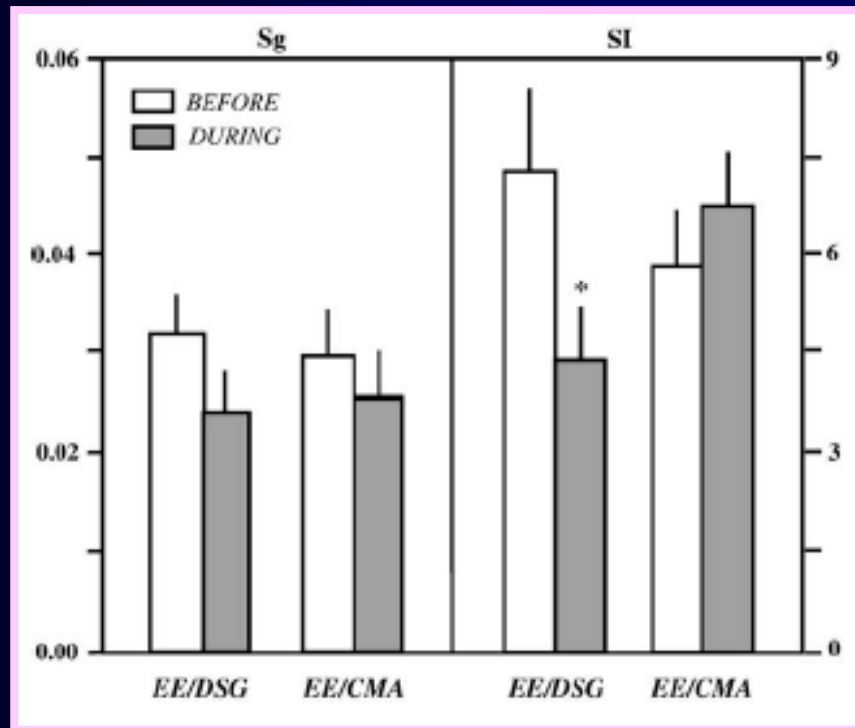


# CMA & IMPATTO METABOLICO

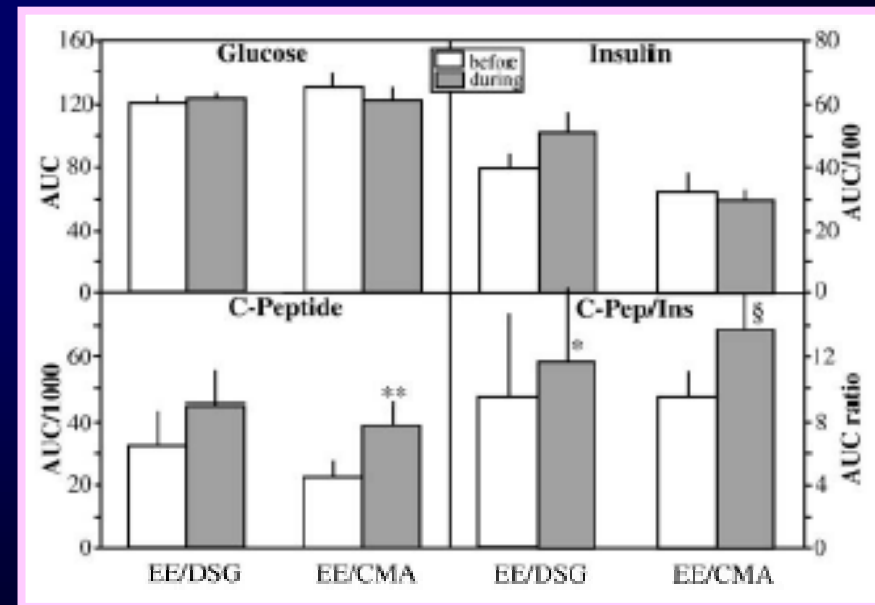
Insulin sensitivity and lipid metabolism with oral contraceptives containing chlormadinone acetate or desogestrel: a randomized trial<sup>☆,☆☆</sup>

❖ Favorevole profilo lipidico del CMA da ricondursi al bilanciamento estrogenico

## SENSIBILITA' INSULINICA



## RISPOSTA PANCREATICA

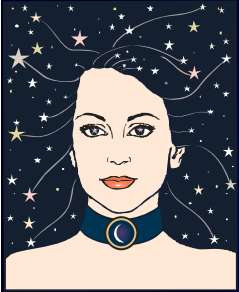


# CMA & DONNE AD ALTO RISCHIO TEV

CMA 10 mg/die, 20 giorni al mese RR = 0.8 (95% IC: 0.2 - 3.9)

	Utilizzatrici CMA n=102	Non Utilizzatrici n=102
Precedenti eventi tromboembolici (ET)	71%	71%
Età precedente evento	26.5 ± 8.0	26.6 ± 7.8
ET superficiale	7	6
ET profondo	60	55
embolia polmonare	18	19
Antecedenti familiari	64	73
fumatrici	No:66/101 Si o Ex : 35/101	No : 60/99 Si o Ex : 39/99
Thrombofilia	44	58
Deficit AT, PS or PC	11	11
FV Leiden	28/97	36/101
mutazione FII	8/91	6/92
sindrome antifosfolipidi	3	8
		<i>Conard et al, 2004</i>



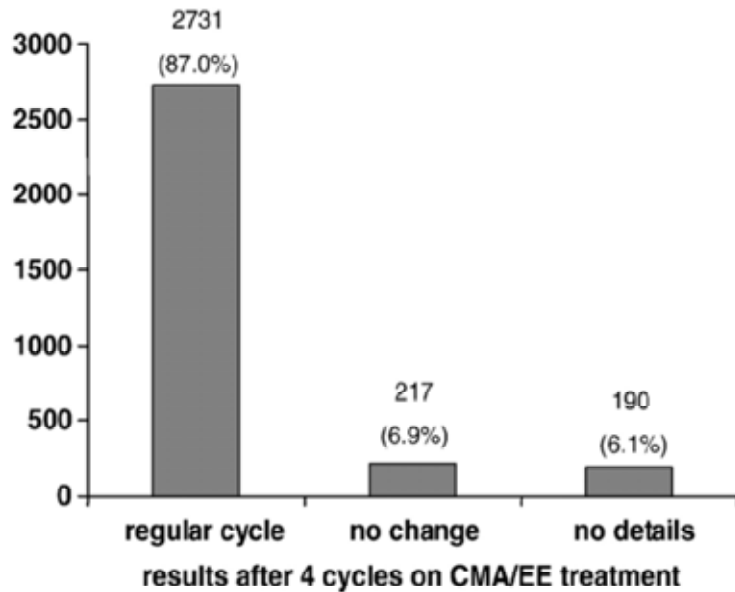


Switching hormonal contraceptives to a chlormadinone acetate-containing oral contraceptive. The Contraceptive Switch Study

# CMA & BENEFICI NON CONTRACCETTIVI

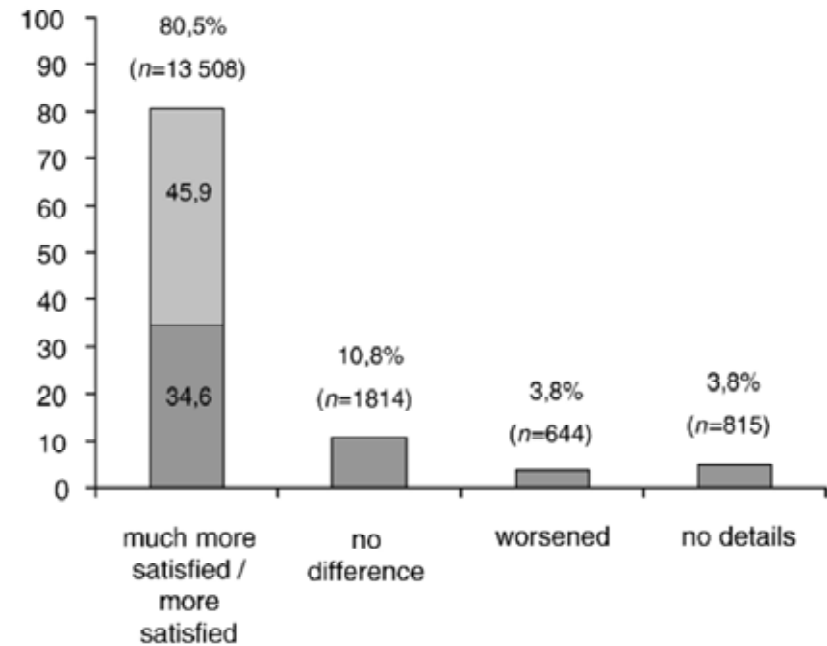
## CONTROLLO DEL CICLO

number of women (total number of women suffering from cycle instability previous to CMA/EE treatment:  $n=3138$ )

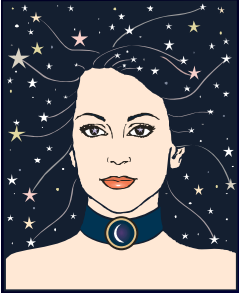


## SENSO DI BENESSERE

women (%)



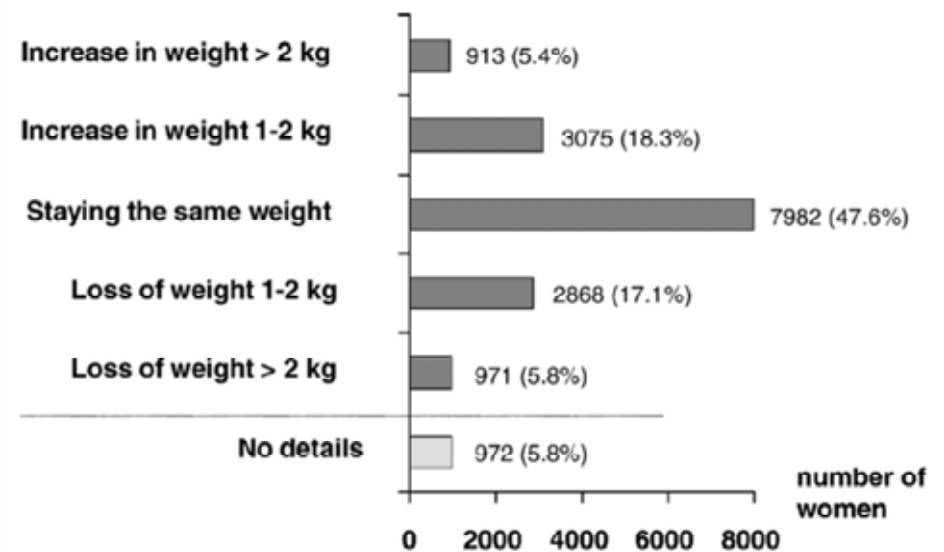
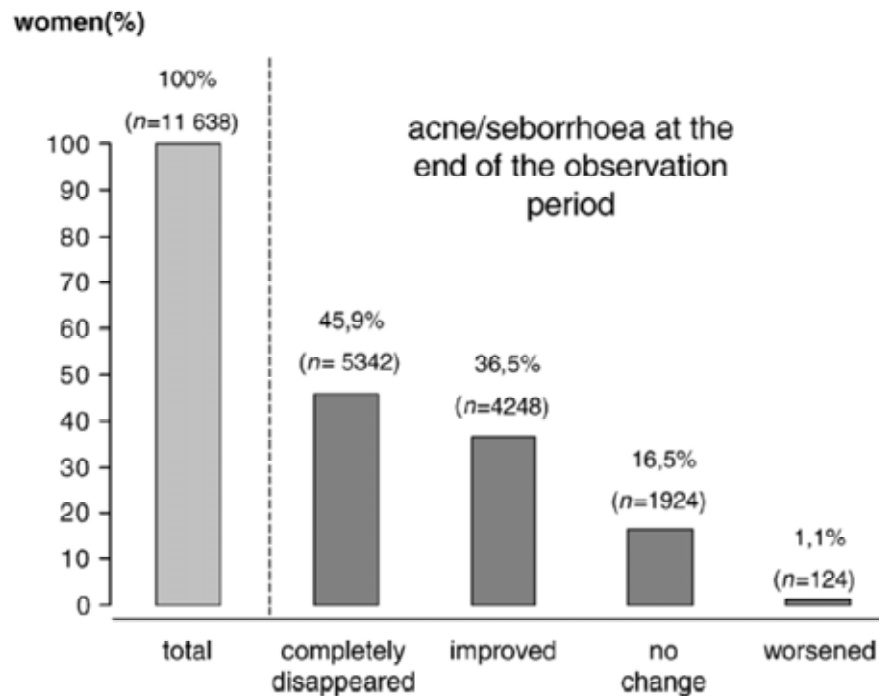
Switching hormonal contraceptives to a chlormadinone acetate-containing oral contraceptive. The Contraceptive Switch Study

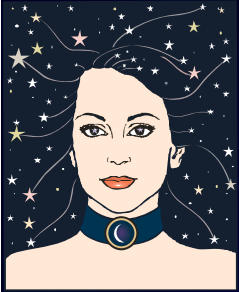


# CMA & BENEFICI NON CONTRACCETTIVI

## ACNE/SEBORREA

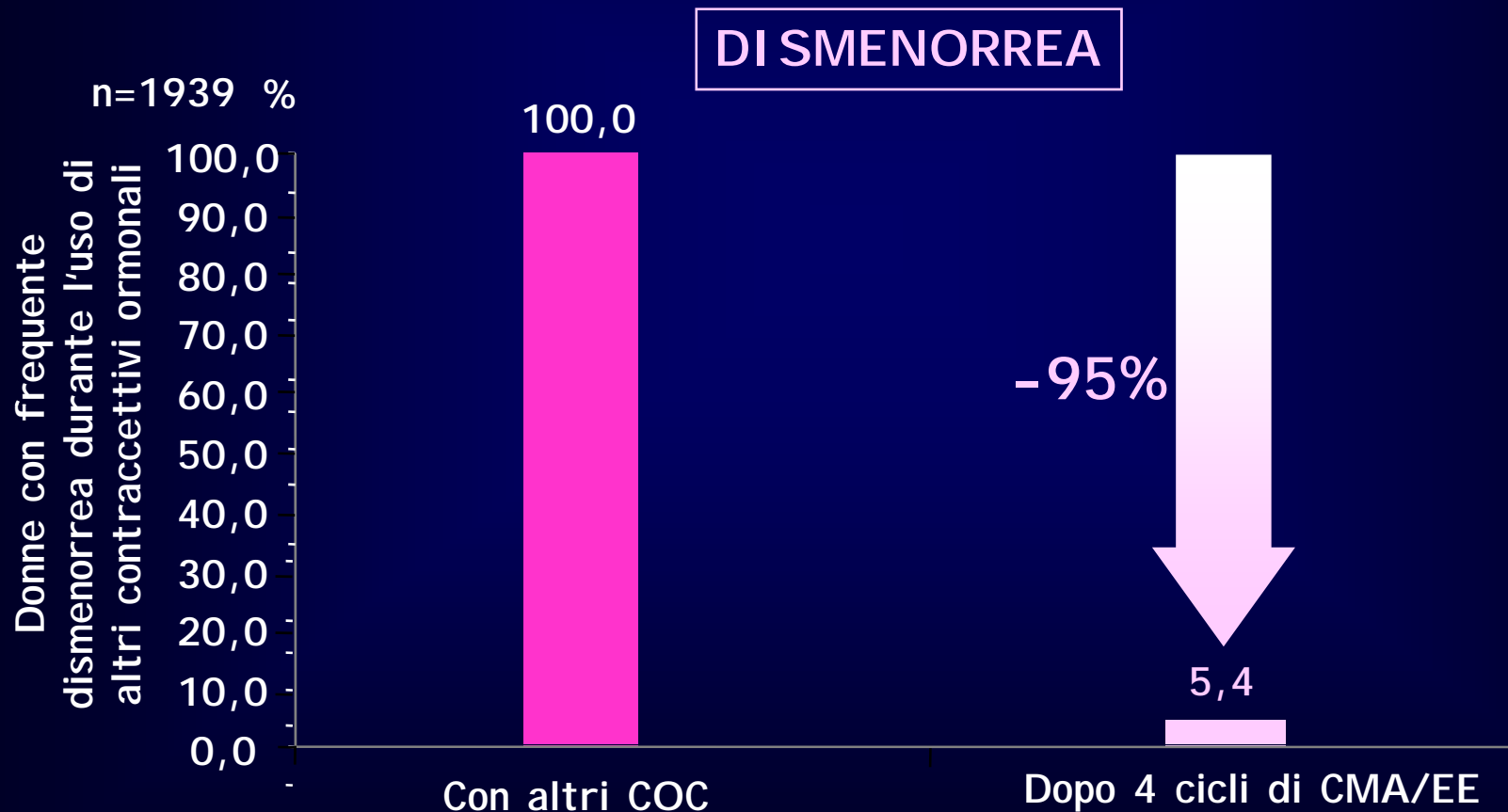
## PESO CORPOREO



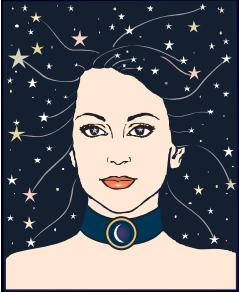


Switching hormonal contraceptives to a chlormadinone acetate-containing oral contraceptive. The Contraceptive Switch Study

## CMA & BENEFICI NON CONTRACCETTIVI



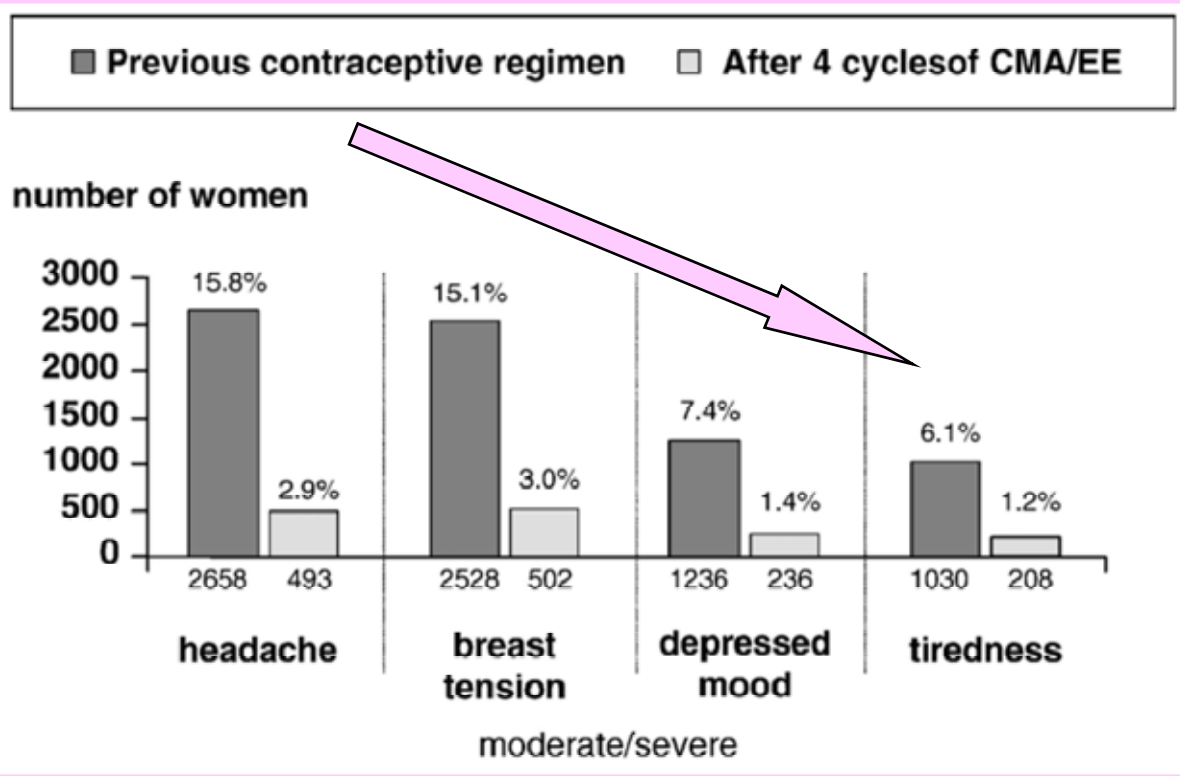
*modificato da Zaharadnik et al 2005; Schramm & Heckes, 2007*



Switching hormonal contraceptives to a chlormadinone acetate-containing oral contraceptive. The Contraceptive Switch Study

# CMA & BENEFICI NON CONTRACCETTIVI

## TONO DELL'UMORE & ALTRI SINTOMI



# CMA & ACNE



Effects of an Oral Contraceptive Containing Chlormadinone and Ethinylestradiol on Acne-Prone Skin of Women of Different Age Groups  
An Open-Label, Single-Centre, Phase IV Study

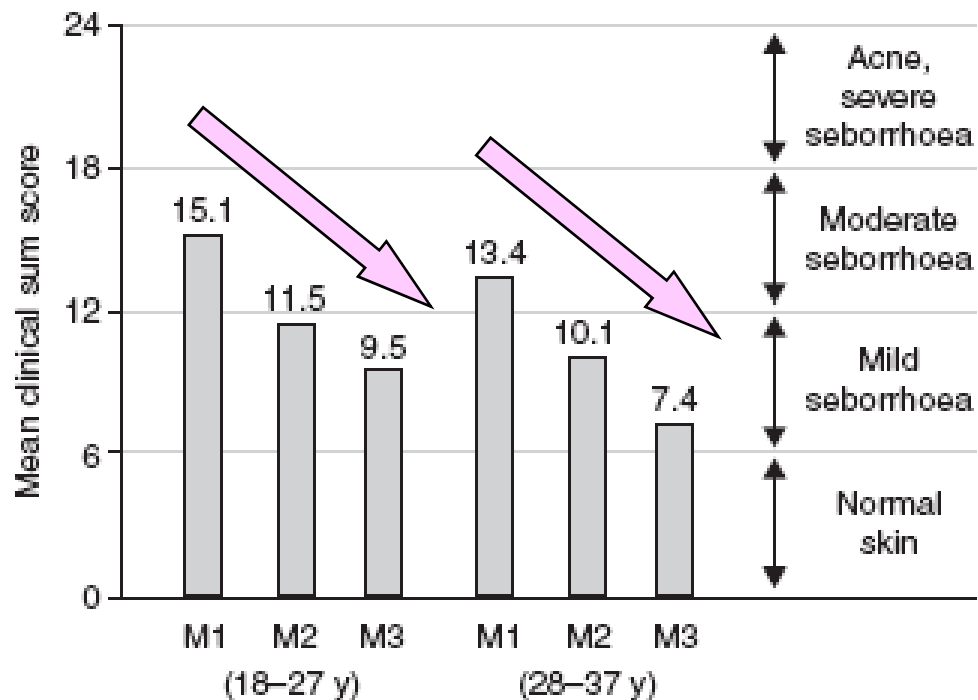
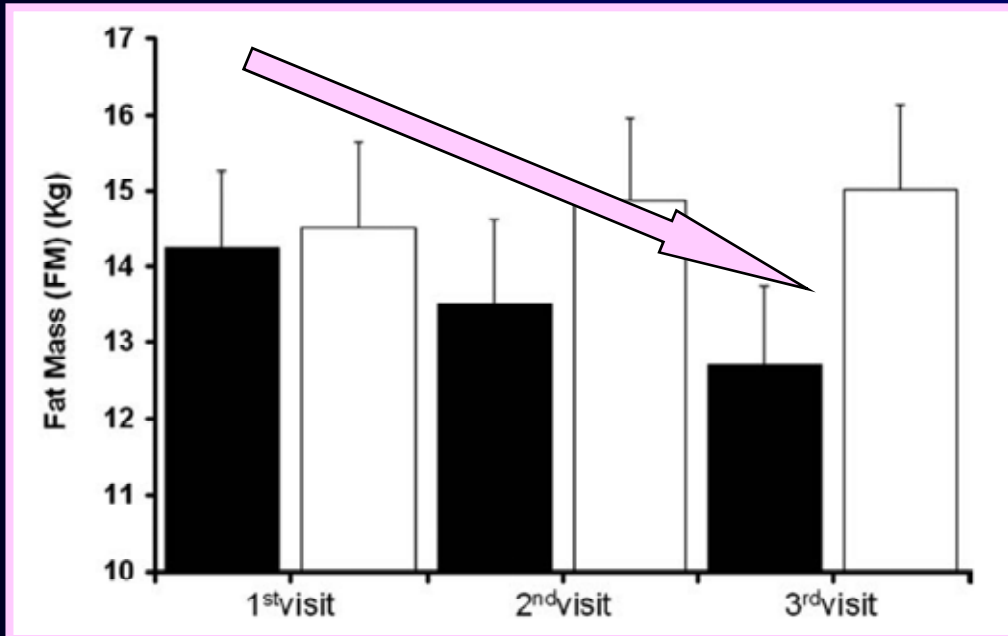
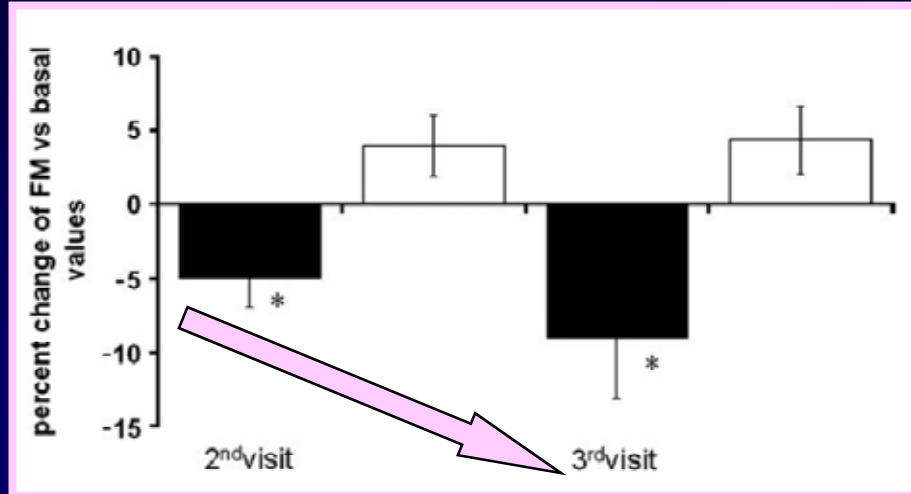


Fig. 1. Improvement in mean clinical sum score of subjects (aged 18-27 years or 28-37 years) with acne-prone skin after three (M2) and six (M3) treatment cycles with chlormadinone/ethinylestradiol. M1 = baseline.

- ❖ Miglioramento di numerosi parametri:
  - aumento idratazione strato corneo
  - riduzione contenuto lipidico della superficie cutanea

# CMA & MASSA GRASSA

Evidence that in healthy young women, a six-cycle treatment with oral contraceptive containing 30 mcg of ethinylestradiol plus 2 mg of chlormadinone acetate reduces fat mass



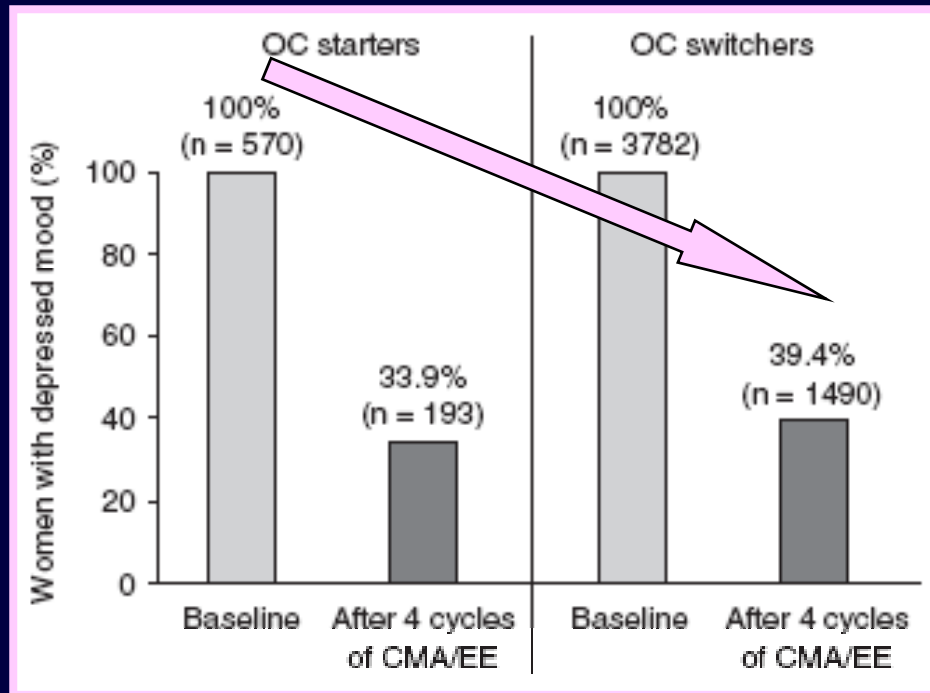
❖ Nessuna modificazione significativa della PA e bilanciamento del CMA degli effetti di EE su aumento di peso e ritenzione idrica



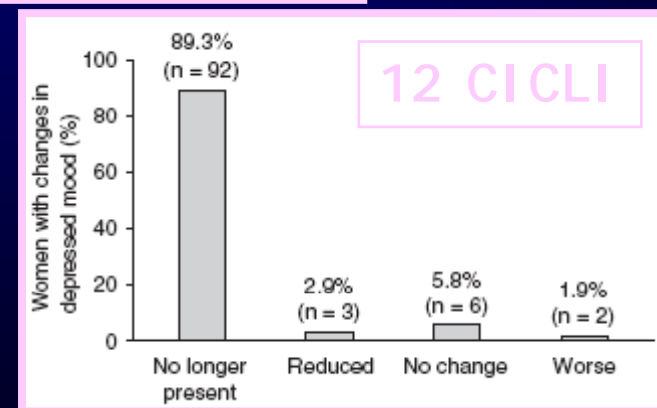
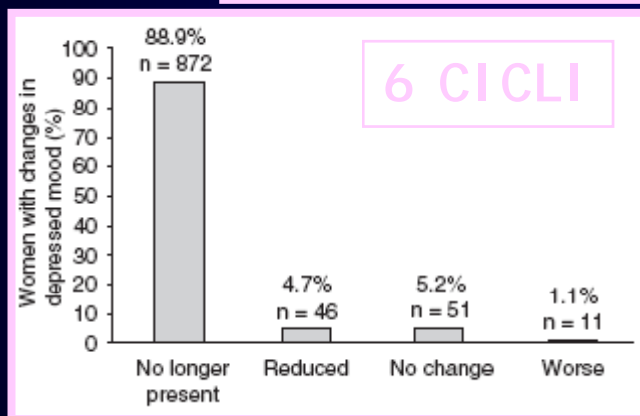
# CMA & TONO DELL'UMORE

## Effect of an Oral Contraceptive with Chlormadinone Acetate on Depressive Mood

Analysis of Data from Four Observational Studies



❖ Alta similitudine strutturale tra un metabolita del CMA e il neurosteroido epipregnanolone



Huber et al, 2008

# NEUROACTIVE STEROIDS

*Synthesized within the CNS by the same steroidogenetic enzymes found in the gonads and the adrenal glands.*

**Progesterone**

5 $\alpha$ -reductase

**5 $\alpha$ DHP**

3 $\alpha$ -HSD

**Allopregnanolone**

**GABA<sub>A</sub> receptor**

*Cl<sup>-</sup> channel openings*

Physiologic neuromodulatory role in

- estrous/menstrual cycle,
- pregnancy,
- stress,
- mood,
- sexual behaviour,
- memory and learning,
- developmental and aging processes

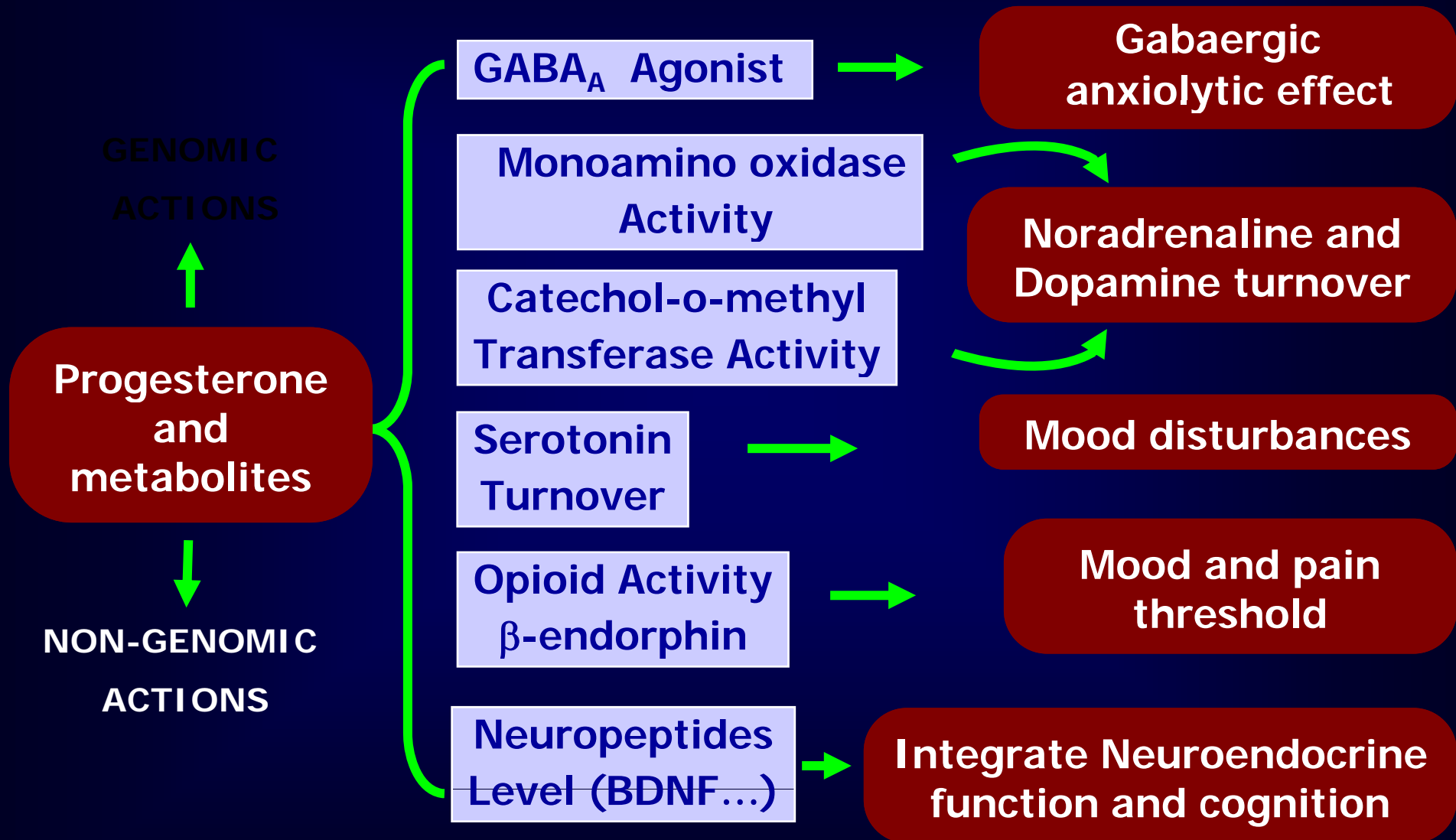
Systemic administration of P

and its metabolites induces

Anxiolytic, Hypnotic and

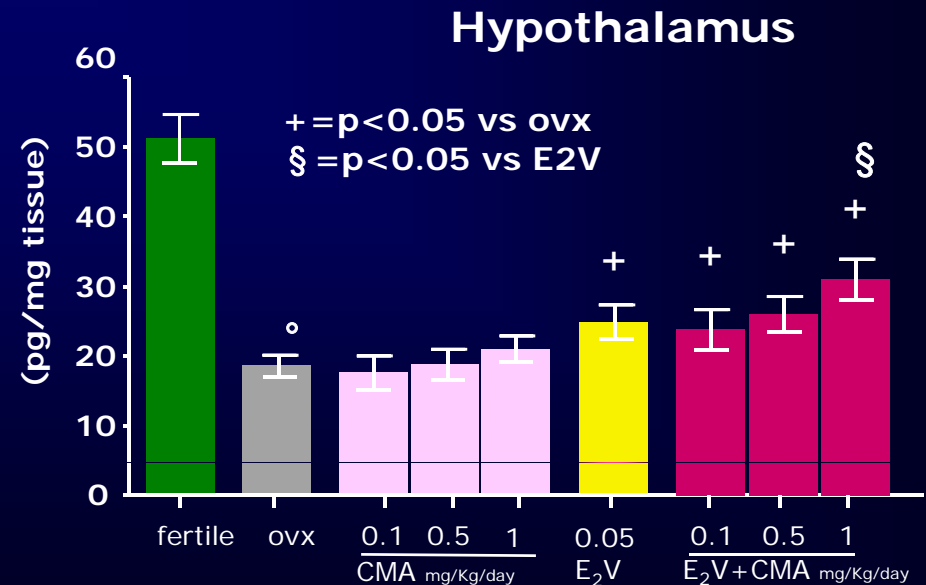
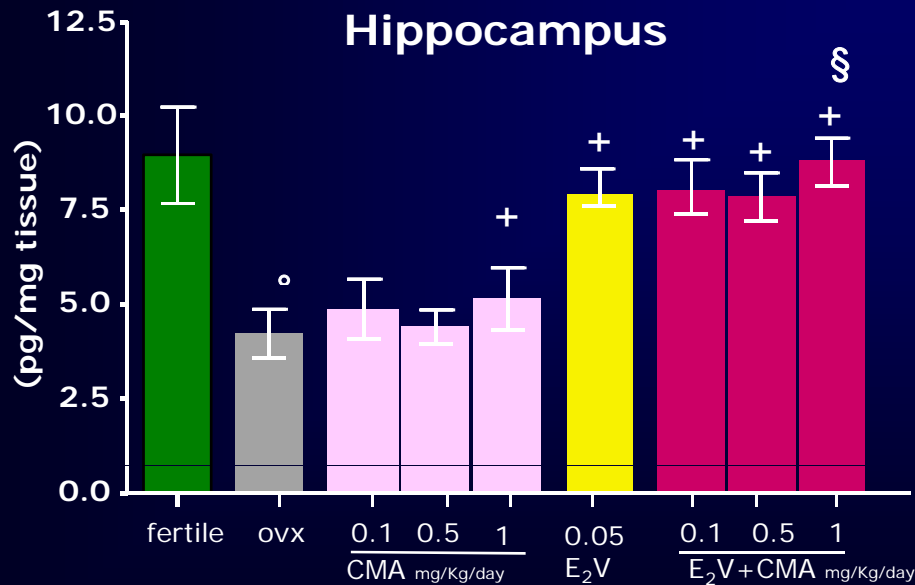
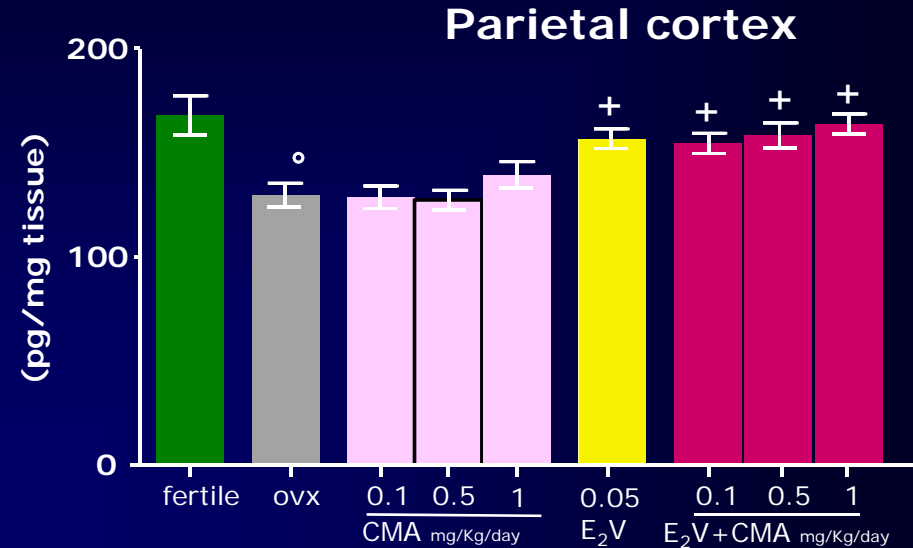
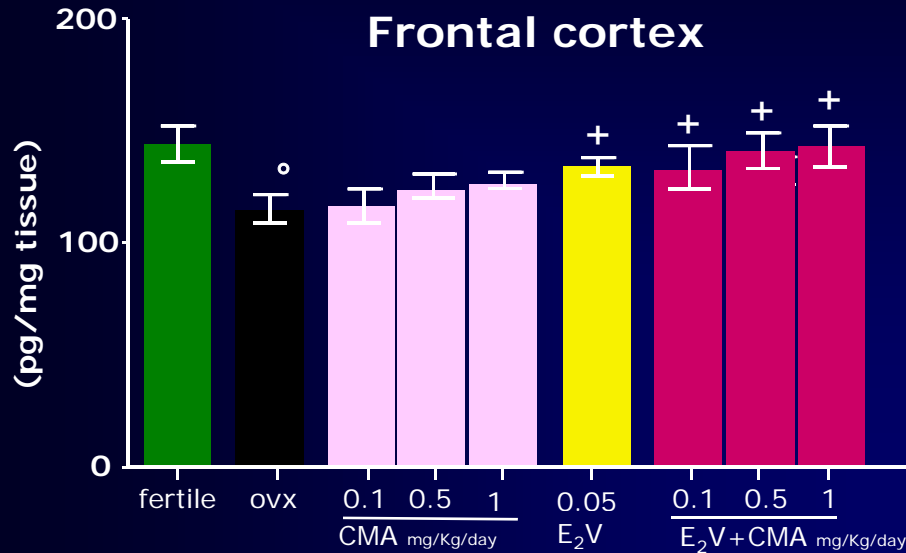
Anticonvulsant effects

# Neuroendocrine effects of Progesterone



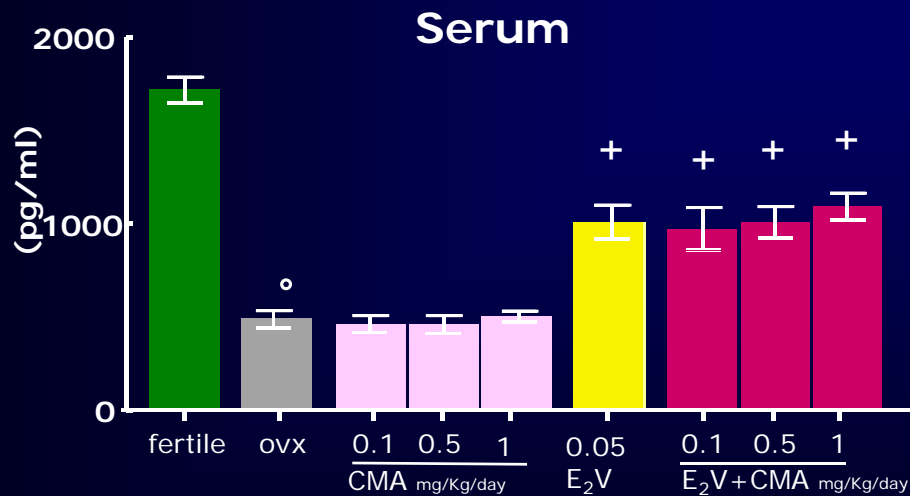
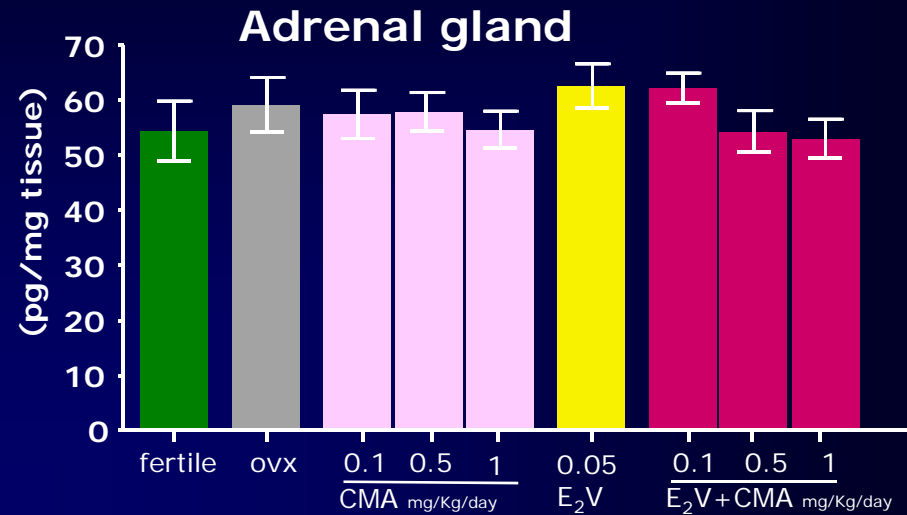
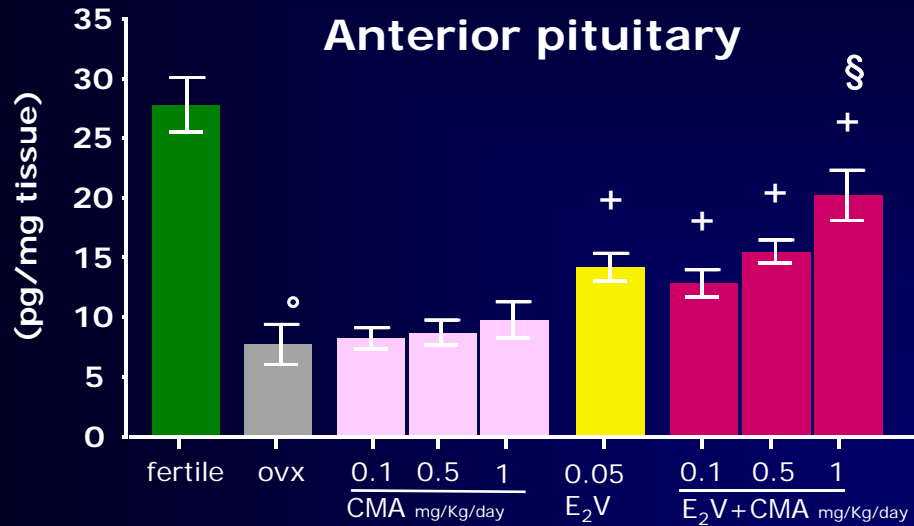
*Courtesy of Andrea R Genazzani & Nicola Pluchino, 2009*

# CMA and Allopregnanolone



*Pluchino et al, in press*

# CMA and Allopregnanolone

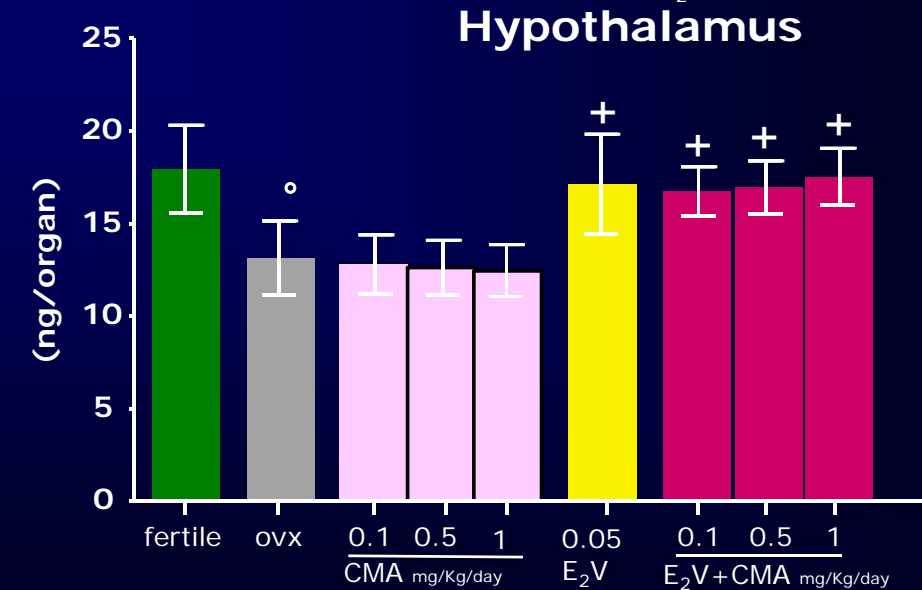
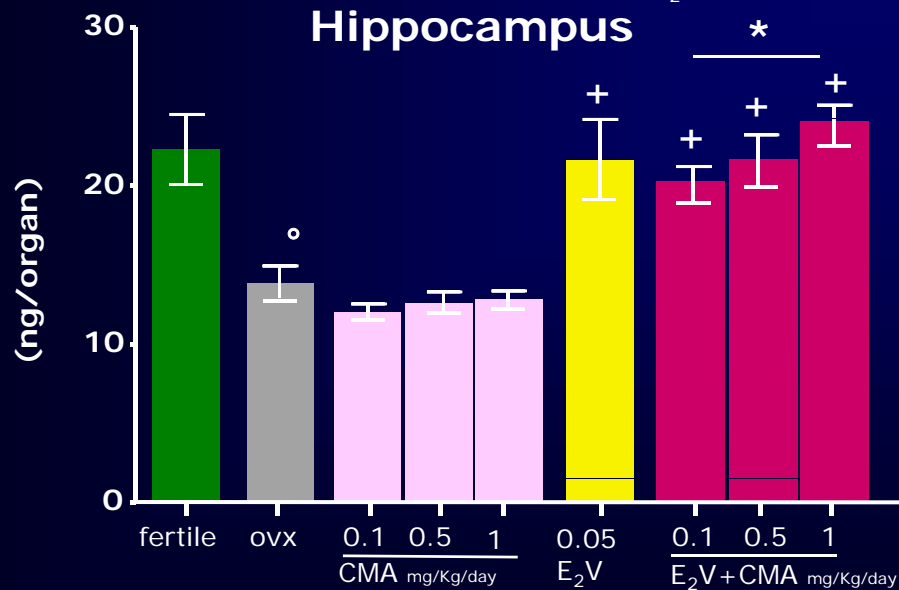
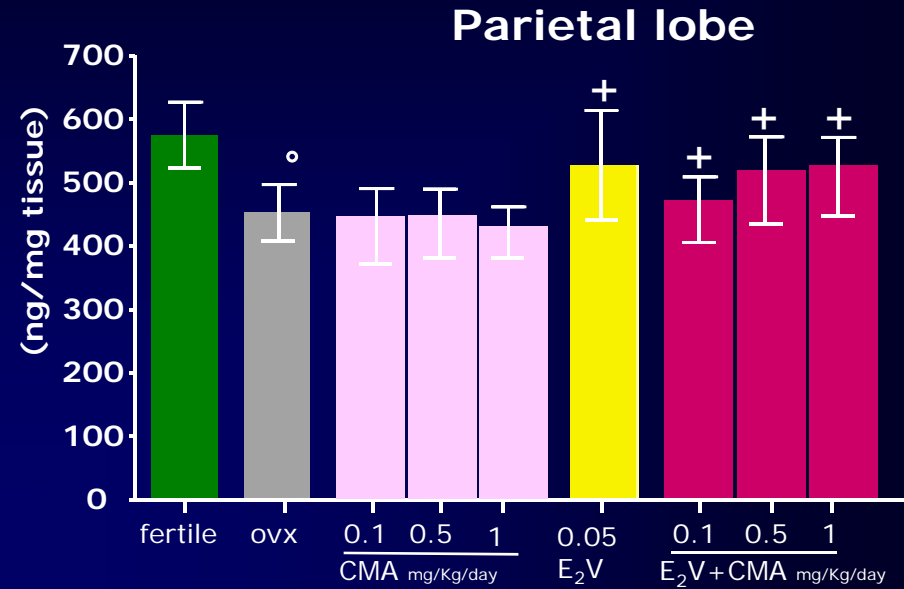
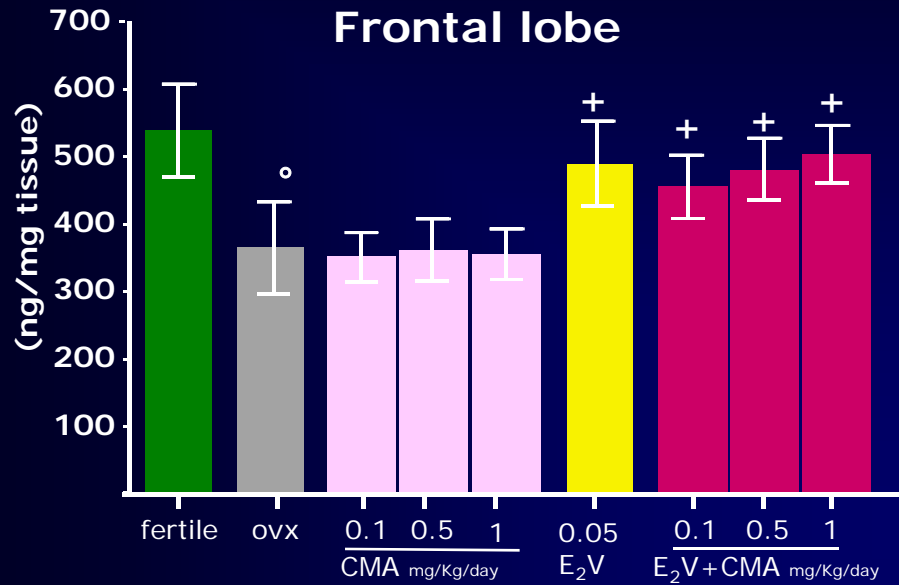


° = p < 0.05 vs fertile

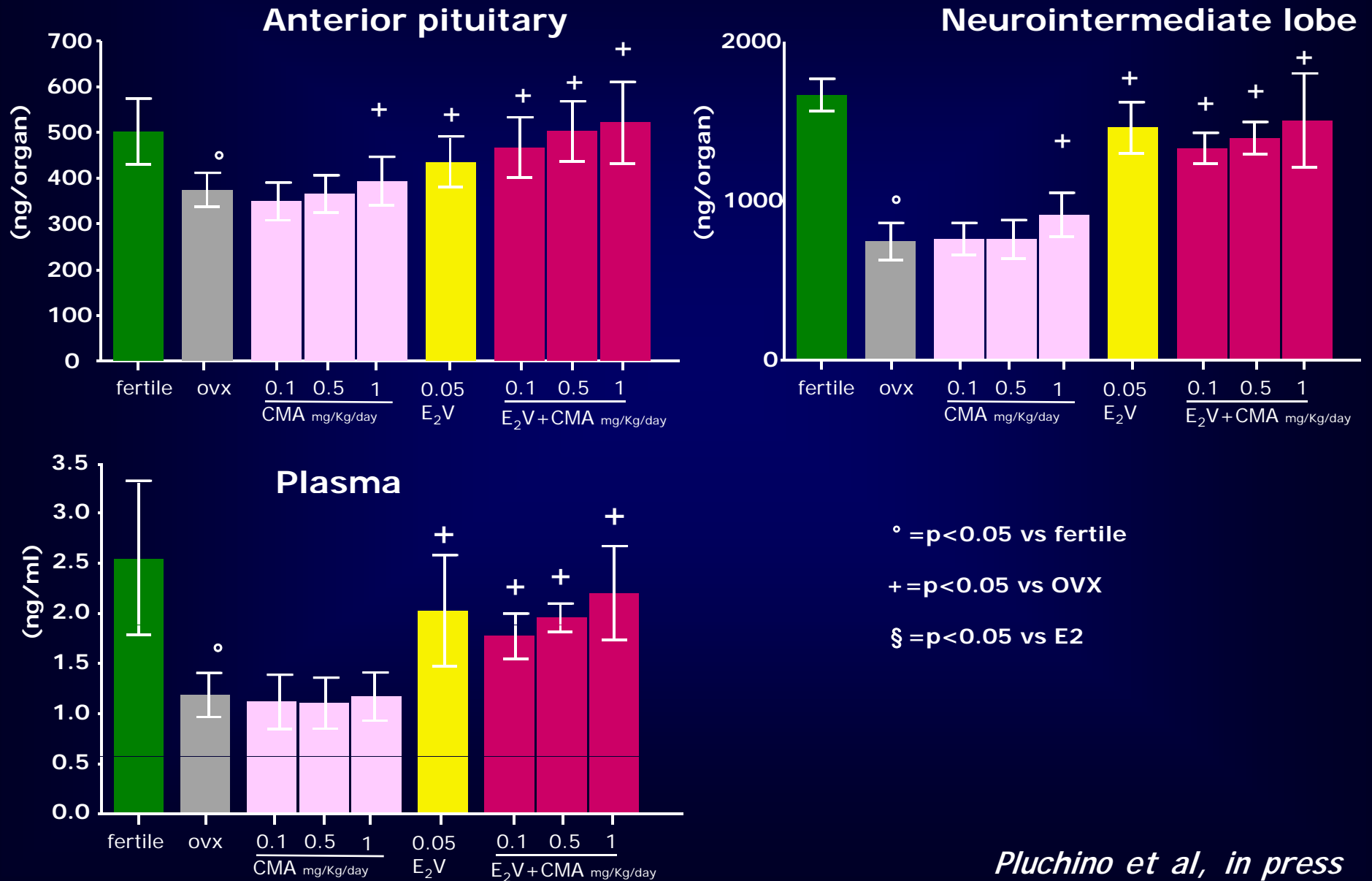
+ = p < 0.05 vs ovx

§ = p < 0.05 vs E<sub>2</sub>V

# CMA and beta-endorphin



# CMA and beta-endorphin



# CMA & SESSUALITA'



Noncontraceptive benefits of two combined oral contraceptives with antiandrogenic properties among adolescents<sup>☆</sup>

❖ Entrambe le formulazioni esercitano effetti positivi sul versante cosmetico e sintomatologico, senza modificare il peso

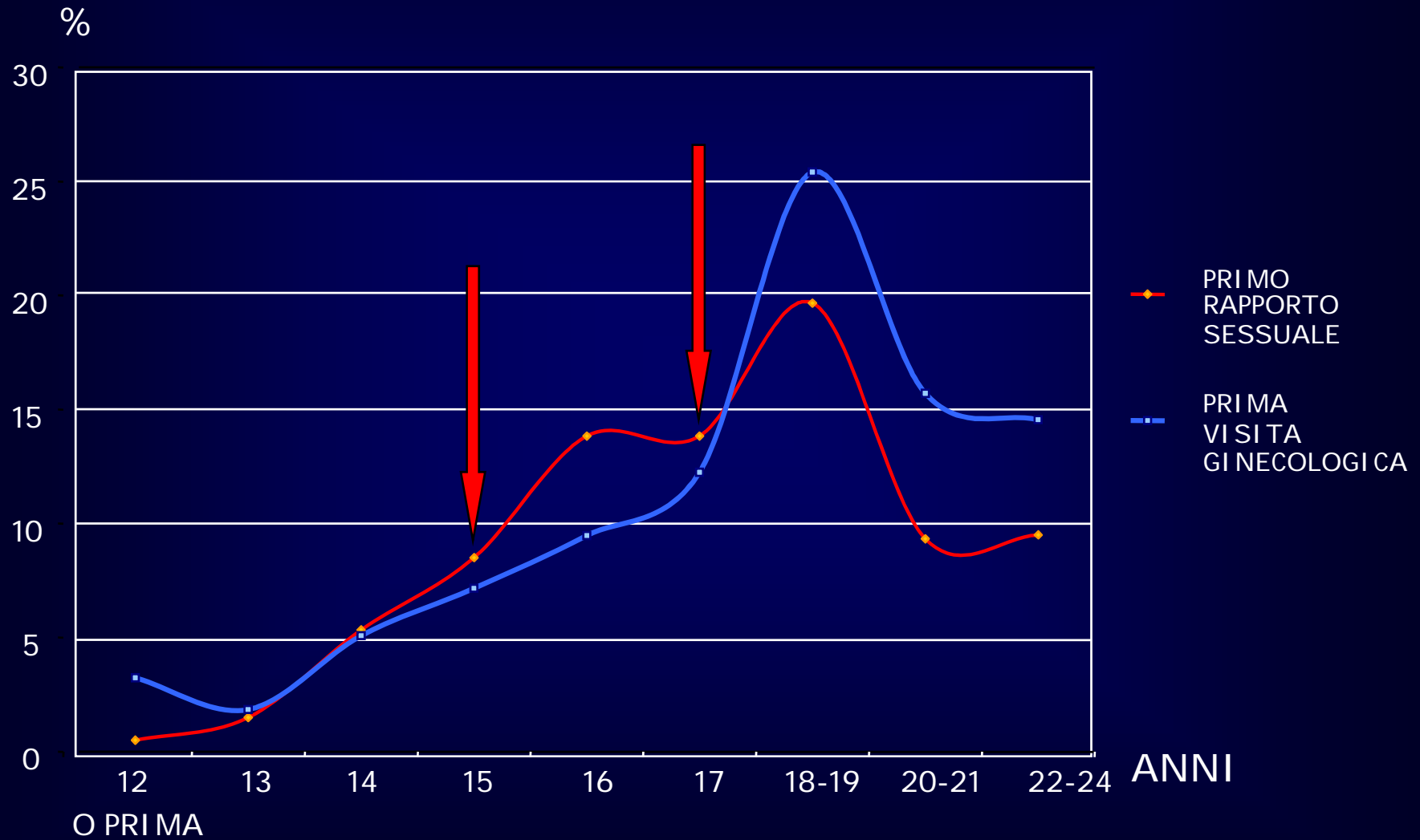
Sexual interest and sexual satisfaction changes in CMA and DRSP users

	Baseline		Cycle 3		Cycle 6		p*
	DRSP	CMA	DRSP	CMA	DRSP	CMA	
<b>Sexual interest</b>							
Poor	22 (28.2)	28 (35.9)	16 (20.5) ↓	12 (15.4) ↓ ↓	20 (25.6) ↓	8 (10.2) ↓ ↓	.001
p			.05	.001	.05	.05	
Moderate	38 (48.6)	36 (46.1)	30 (38.4)	34 (43.5)	33 (42.3)	38 (48.6)	.01
p			.01	n.s.	n.s.	n.s.	
High	18 (23.1)	14 (17.9)	25 (32.1)	32 (41.0)	25 (32.0)	32 (41.0)	.01
p			.05	.001	n.s.	n.s.	
<b>Sexual satisfaction</b>							
Poor	44 (56.4)	41 (52.5)	26 (33.3)	21 (26.9)	22 (28.2)	18 (23.1)	.001
p			.001	.001	.05	.05	
Moderate	18 (23.1)	20 (25.6)	34 (43.5)	32 (41.0)	33 (42.3)	30 (38.4)	.001
p			.001	.001	n.s.	n.s.	
High	16 (20.5)	17 (21.8)	18 (23.1)	25 (32.0) ↑ ↑	23 (29.4) ↑	30 (38.4) ↑ ↑	.001
p			n.s.	.01	.05	.01	

The data are reported as n (%).

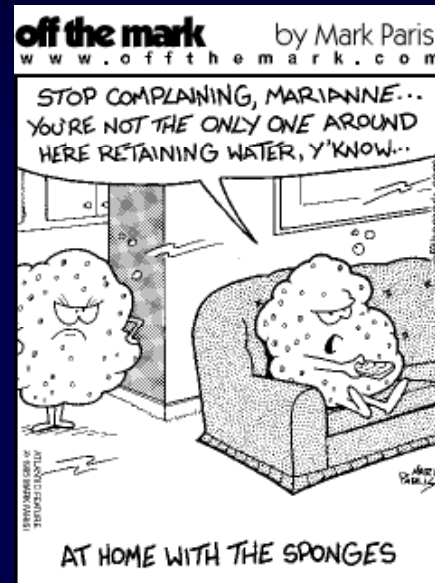
\* p value, CMA versus DRSP at Cycle 6.

# ETA' DEL PRIMO RAPPORTO SESSUALE & DELLA PRIMA VISITA GINECOLOGICA



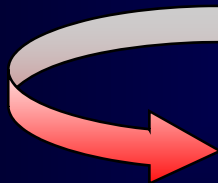
*Cortesia di E Finzi, ASTRA RICERCHE, 2008*

# TAILORING OF OPTIONS IN HORMONAL CONTRACEPTION

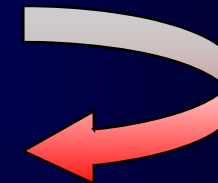


CHOICE IS  
FREEDOM

COUNSELLING IS  
KNOWLEDGE



❖ ACTIVE ROLE IN  
REPRODUCTIVE & SEXUAL  
WELL-BEING



❖ TREATING SYMPTOMS &  
PREVENTION OF DISEASES