

Menstrual cycle disorders

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Definitions

■ Secondary amenorrhea

- 3 consecutive months without periods

■ Primary amenorrhea

- No periods after the age of 16 – 17

■ Hypomenorrhea

- Periods < 3 days with little bleeding

Definitions

■ Menorrhagia

- Periods > 7 days & > 80 ml

■ Hypermenorrhea

- Periods > 80 ml

■ Oligomenorrhea

- Cycle > 35 days

■ Polymenorrhea

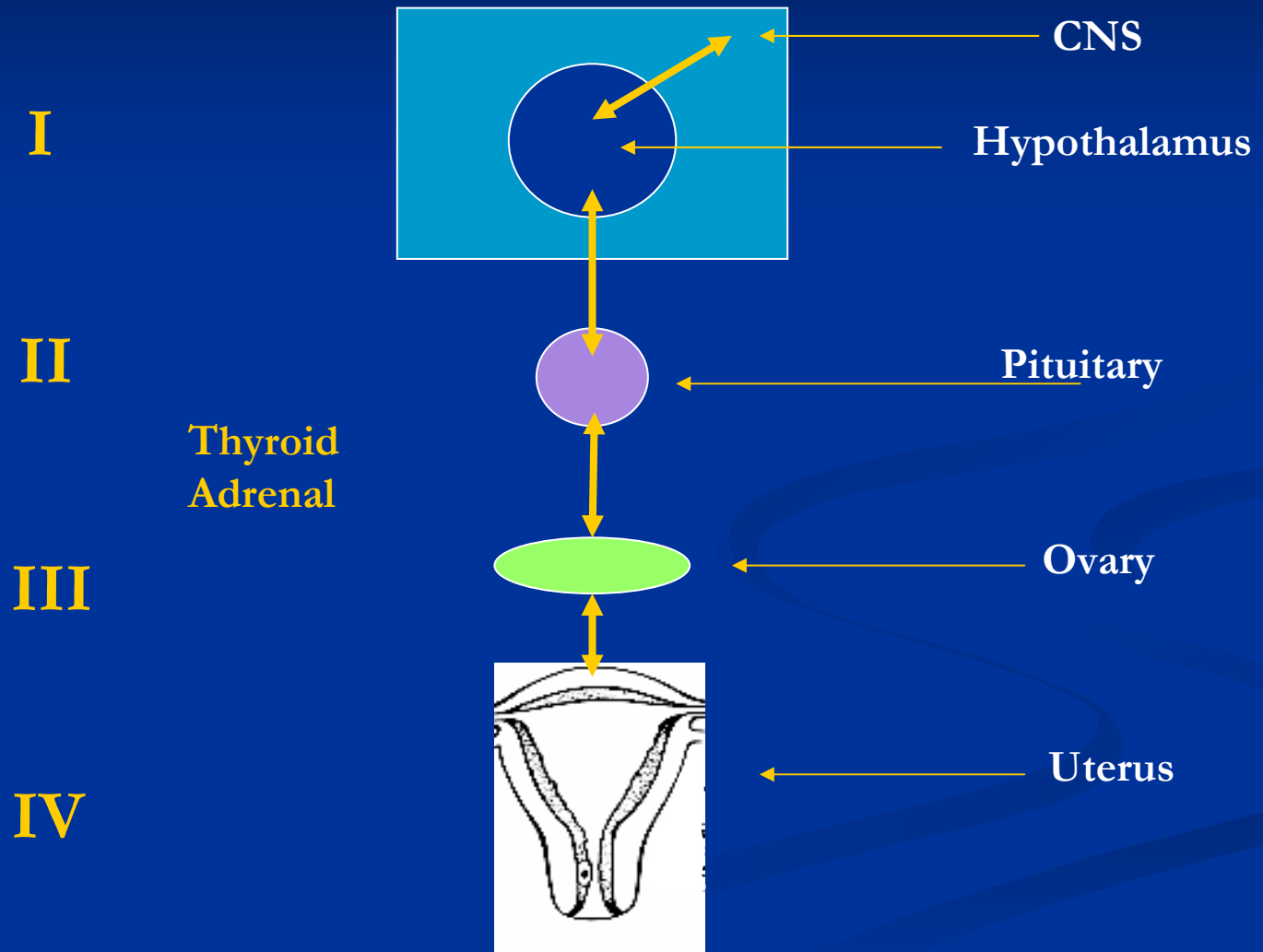
- Cycle < 21 days

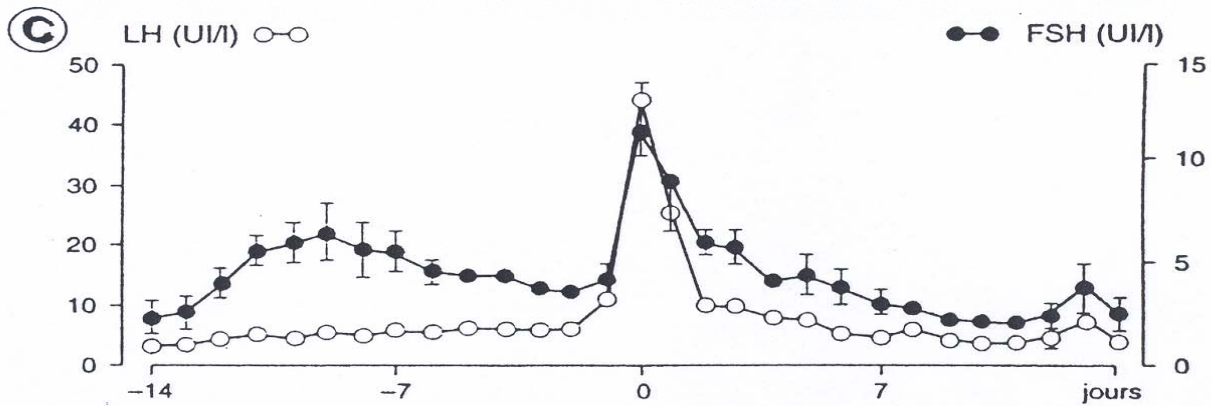
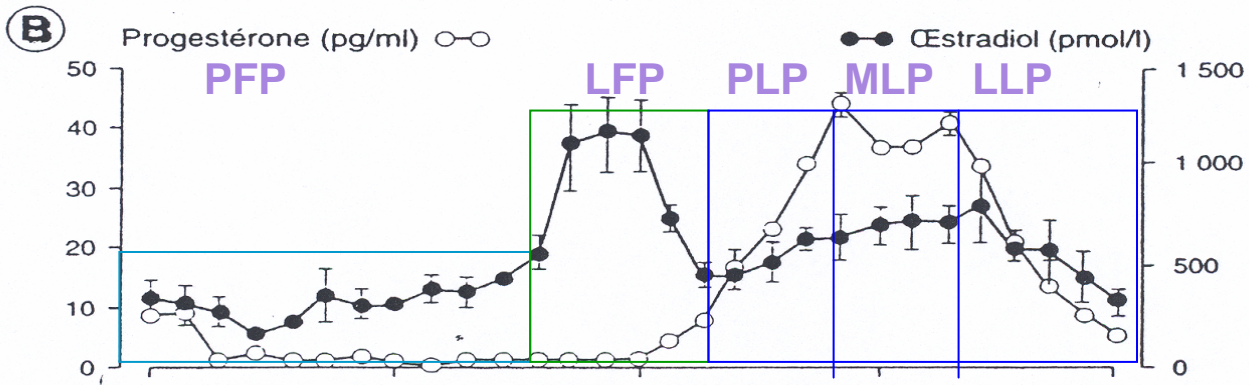
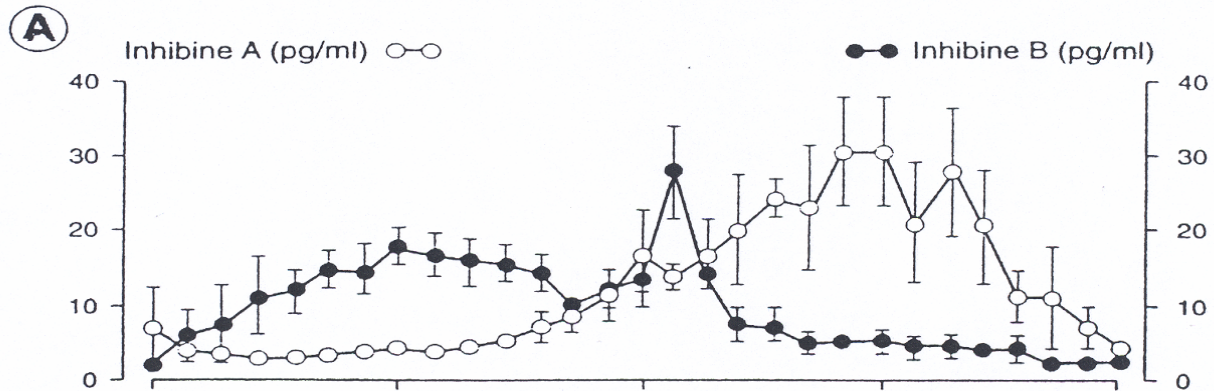
Definitions

- **Primary dysmenorrhea**
 - Painful periods before the age of 19

- **Secondary dysmenorrhea**
 - Painful periods after the age of 19

Different levels

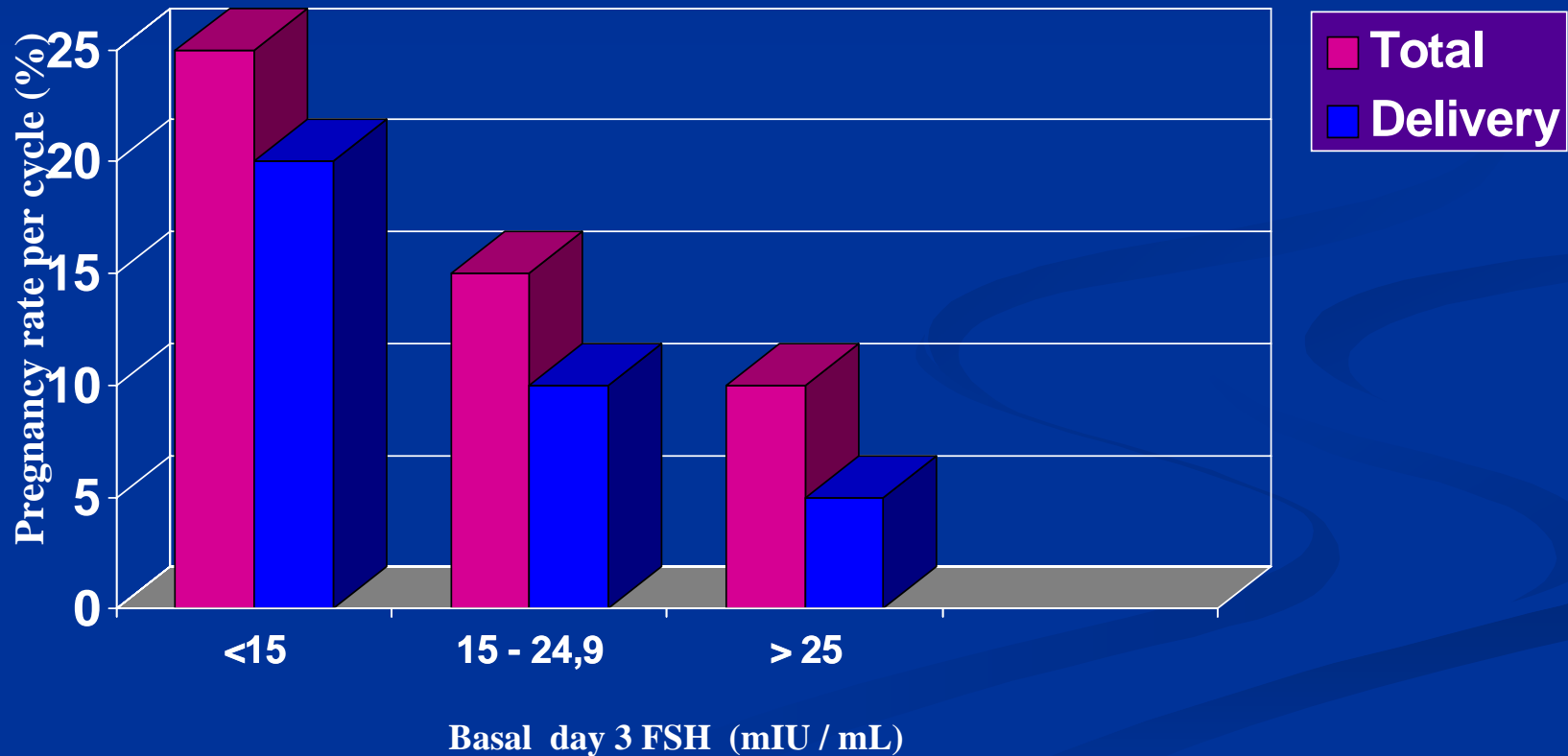




Hormonal assays: FSH

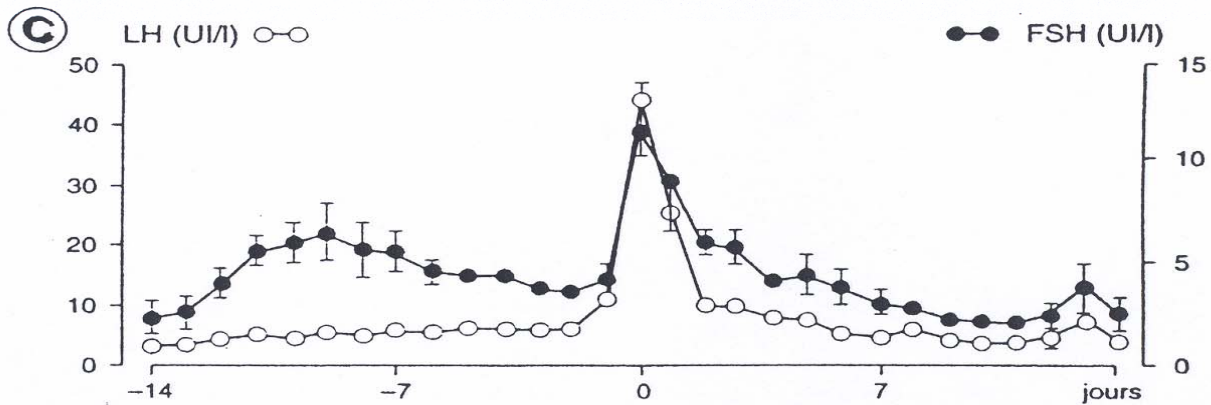
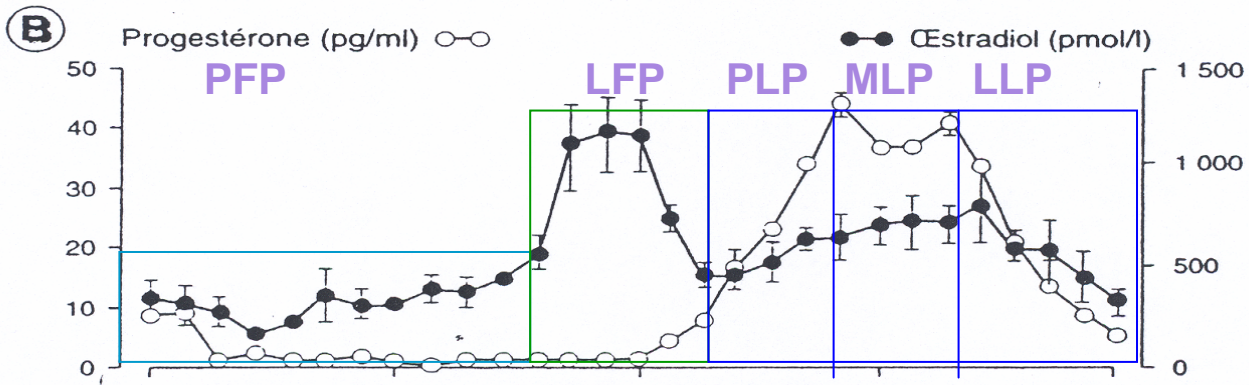
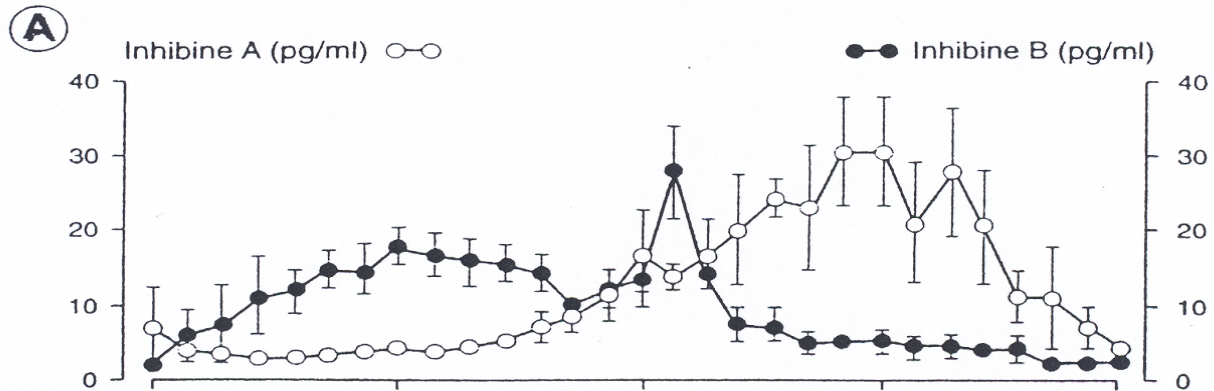
Prognostic value of day 3 FSH levels in 758 patients undergoing an IVF cycle

Adapted from Scott et al. 1989, Fertil. Steril., 51 651 -654



Hormonal assays: LH

- Day 3
- $\text{LH} > 10 \text{ IU/L}$, or $\text{LH/FSH} > 2.5$
 - infertility
 - spontaneous abortions
 - PCOS



Basal Body Temperature

- \uparrow basal body temperature $\geq 0.2^{\circ}\text{C}$
- \uparrow basal body temperature ≥ 12 days

Basal Body Temperature

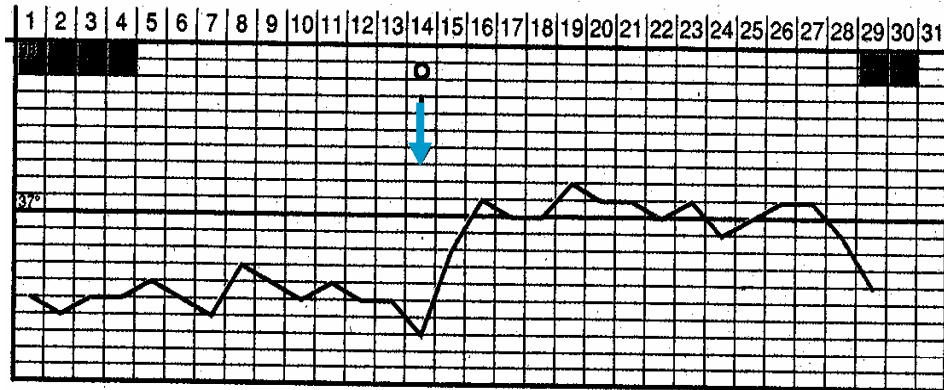
- Inexpensive
- Repeated in different cycles
- Not appropriate to time ovulation
- Poor correlation with P level and endometrial biopsies

Basal body temperature

Jours du cycle

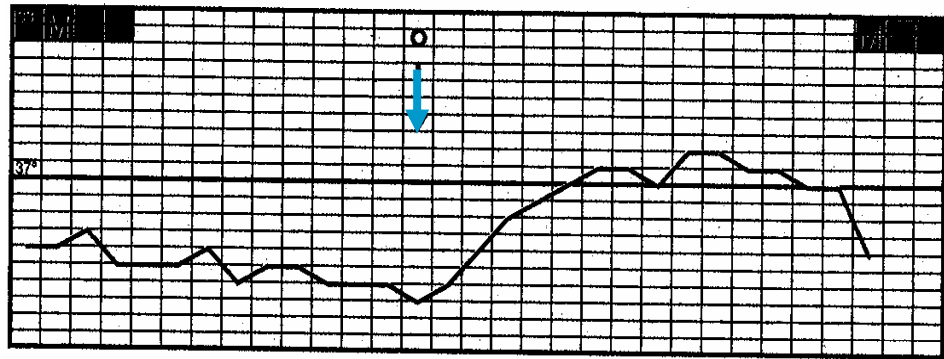
A

Courbe thermique au cours d'un cycle normal de 28 jours.
Ovulation au 14^e jour. Décalage thermique franc.



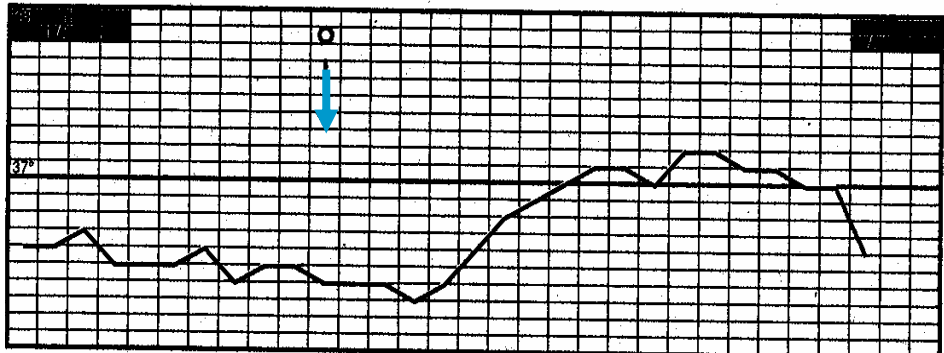
B

Courbe thermique au cours d'un cycle normal de 28 jours.
Ovulation au 14^e jour. Décalage thermique progressif.



C

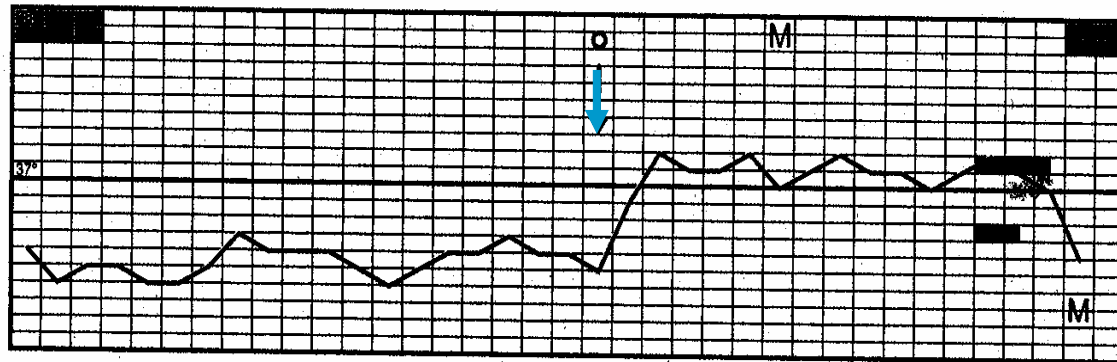
Cycle de durée différente.
La menstruation survient toujours 12 à 14 jours après l'ovulation.
Cycle de 25 jours. Ovulation au 11^e jour.



Basal body temperature

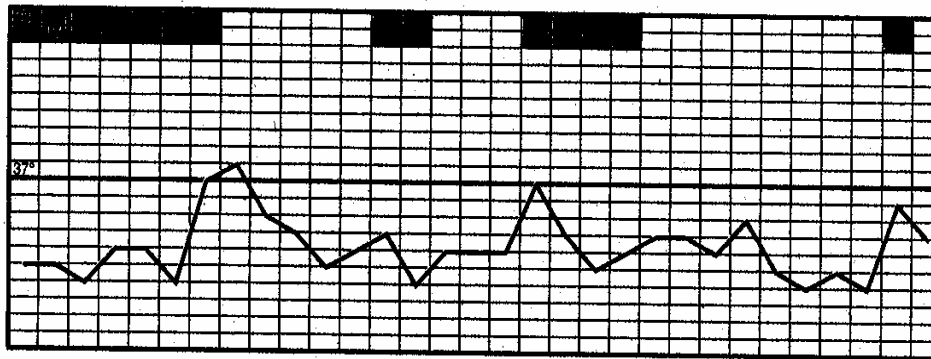
D

Cycle de 35 jours. Ovulation au 21^e jour.



E

Métrorragies fonctionnelles sur courbe thermique monophasique. La courbe thermique sans décalage thermique prolongé objective l'absence d'ovulation.

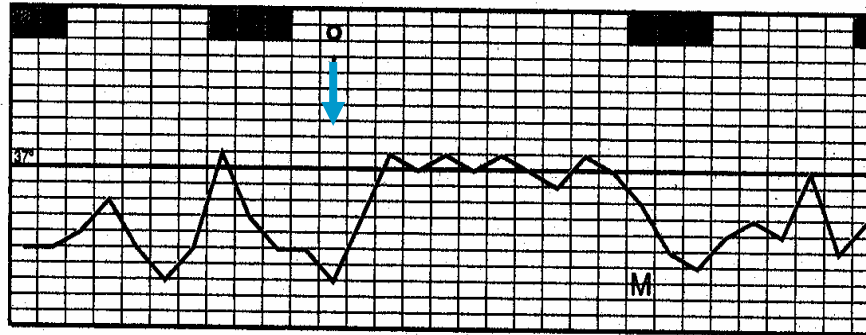


- date théorique de l'ovulation
- saignement génital
- M menstruation
- ⊕ test de grossesse positif

Basal body temperature

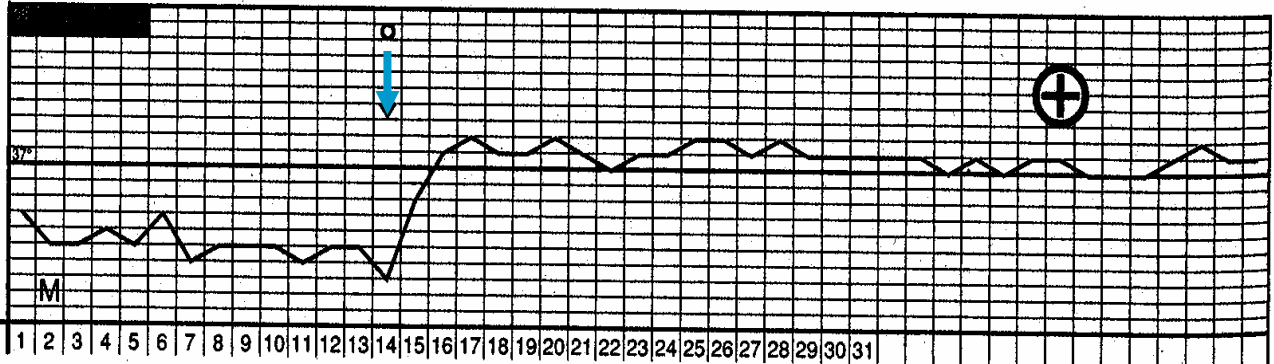
F

Ménométrorragies.
La courbe thermique permet de distinguer la survenue d'une menstruation vraie (M) des autres saignements génitaux.



G

Début de grossesse.
Ovulation au 14^e jour. Persistance du plateau thermique avec absence de menstruation. Test de grossesse positif 10 jours après la date des règles « manquantes ».



Hormonal assays: Progesterone

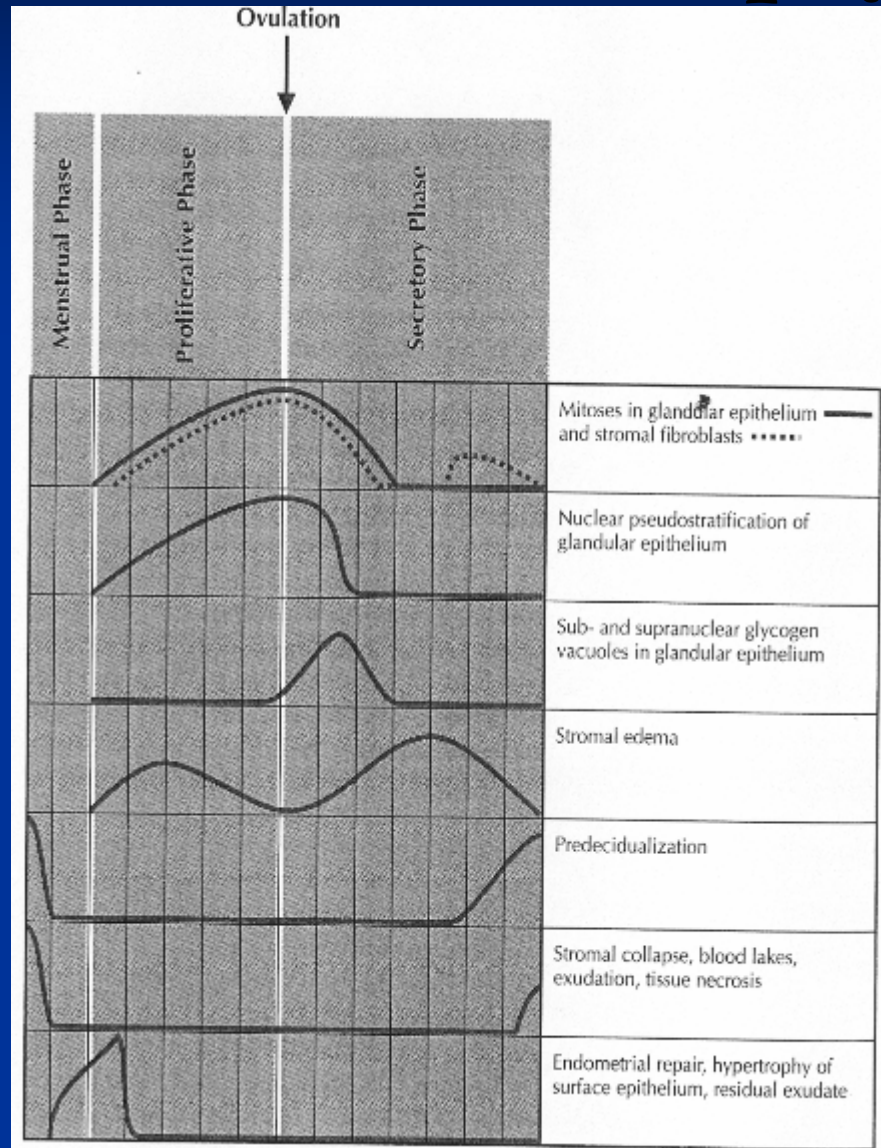
■ Day 21

- 2.5 - 5 ng / ml ovulation
- 10 - 15 ng / ml normal corpus luteal function

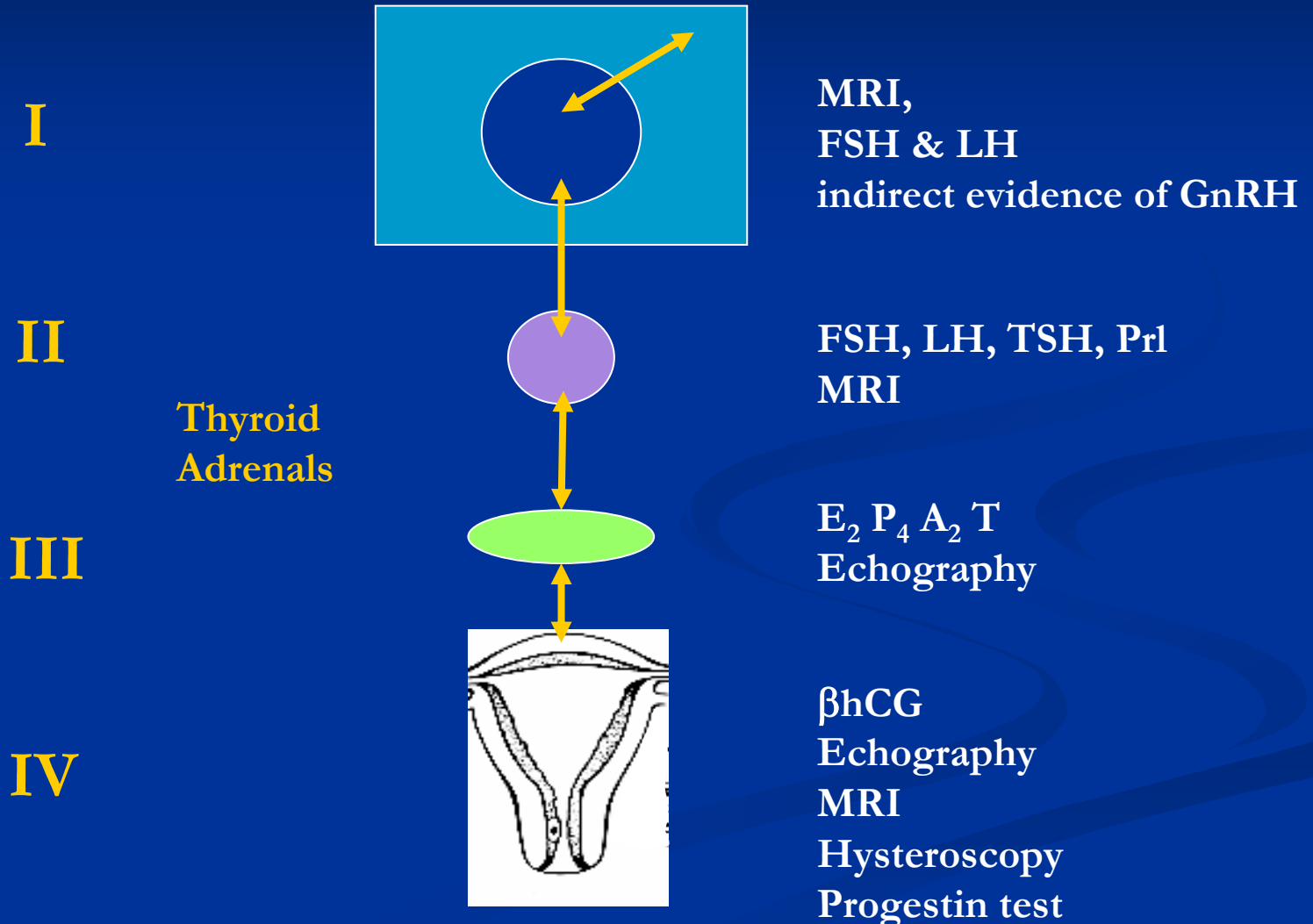
■ Day 20, 21, 22

- $\Sigma : 15 \geq \text{ng/ ml}$

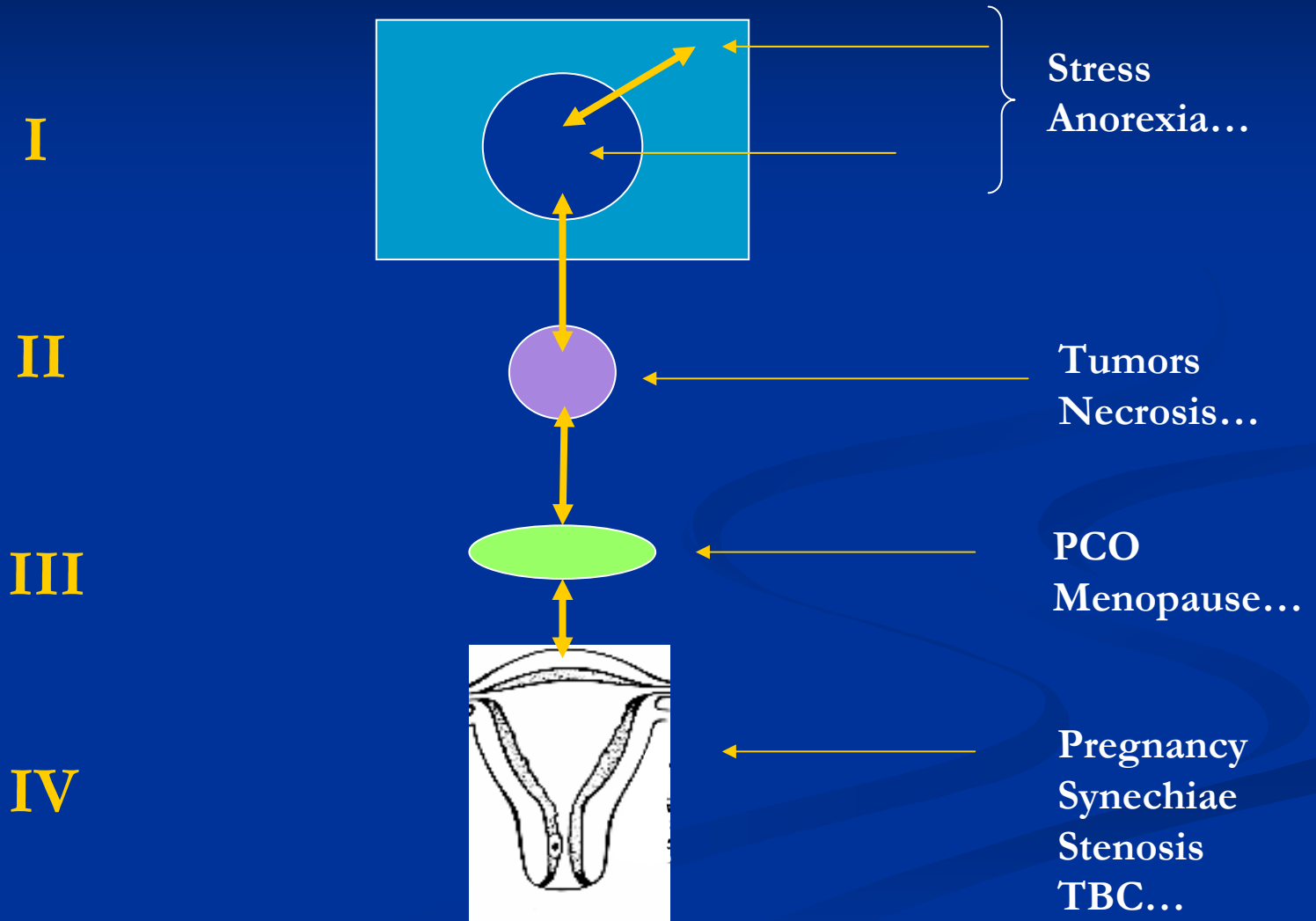
Endometrial biopsy



Different levels



Some etiologies of secondary amenorrhea



Investigating secondary amenorrhea

- Exclude pregnancy
- normogonadic amenorrhea
 - $E_2 > 30$ pg/ml
- Hypogonadic amenorrhea
 - $E_2 < 30$ pg/ml
 - Hypergonadotropic (primary hypogonadism)
 - $FSH > 20 - 30$ UI/L
 - Hypogonadotropic (secondary hypogonadism)
 - $LH < 1$ UI/L

Case 1

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months)
- Investigations
 - Pregnancy test –
 - E₂ 25 pg/ml
 - FSH = 2 UI/L, LH 0.2 UI/L Prl N
- Diagnosis: Hypogonadotropic hypogonadism
hypothalamic amenorrhea
- Cave bone mass

Case 2

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months) hot flushes
- Investigations
 - Pregnancy test –
 - E₂ 25 pg/ml
 - FSH = 52 UI/L, LH 25 UI/L Prl N
- Diagnosis
 - Hypergonadotropic hypogonadism: precocious menopause

Case 2

- Other investigations
 - Test other endocrine pathways
 - Test for autoimmune diseases
 - Test for genetic diseases (X fragile, Turner....)
- Counselling
- THS

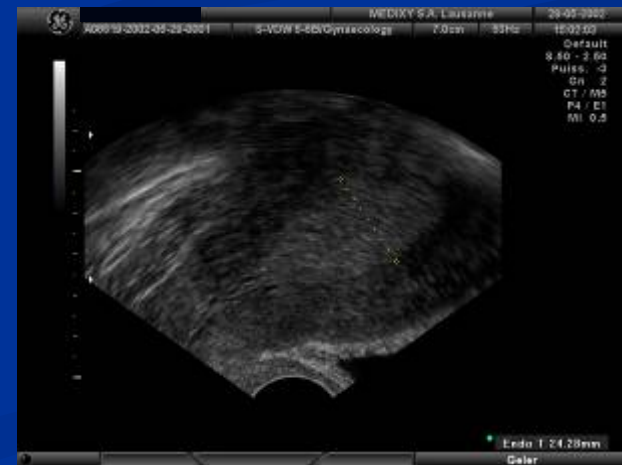
Case 3

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months) History of irregular cycles
- Investigations
 - Pregnancy test –
 - E₂ 105 pg/ml
 - FSH = 4 UI/L, LH 14 UI/L Prl N
- Diagnosis
 - « Normogonadic » amenorrhea

Case 3

■ Investigations

- T = 0.9 ng/ml
- 17 OH-P = 250 ng/dl
- ACTH testing
 - 17 OH-P = 450 ng/dl
- Ultrasound



PCO

?

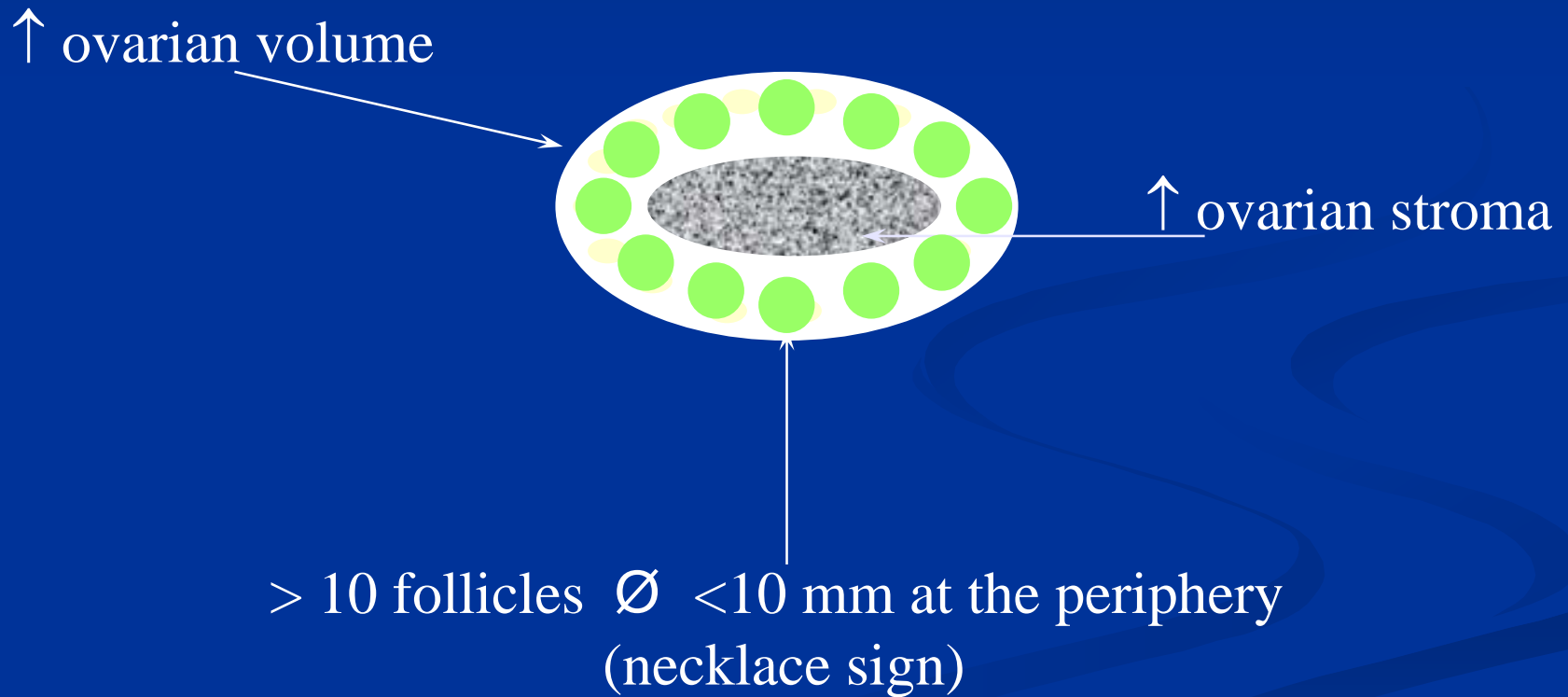
PCOS



- Ultrasound criteria

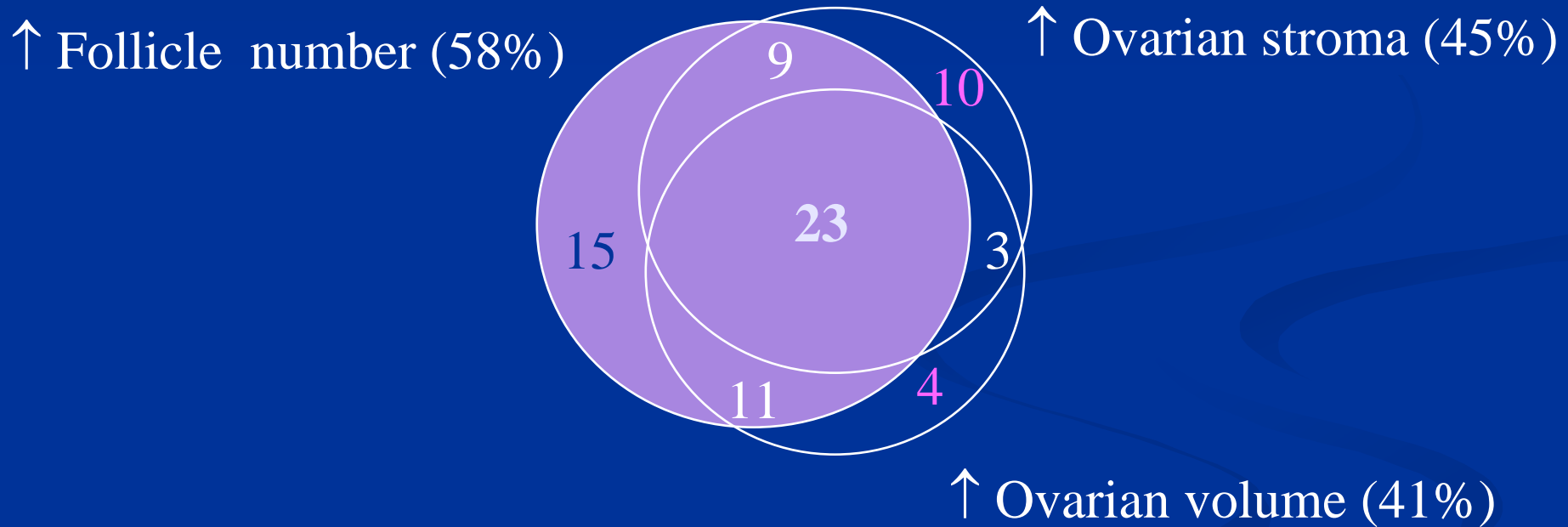
- Infertility 88 %
- Insulin resistance 70 %
- Hirsutism 62 %
- Irregular cycles 50 %
- Obesity 38 %
- Acne 35 %

PCO and ultrasound criteria



PCO and ultrasound criteria

van Santbrink et al. 1997 Fertil Steril



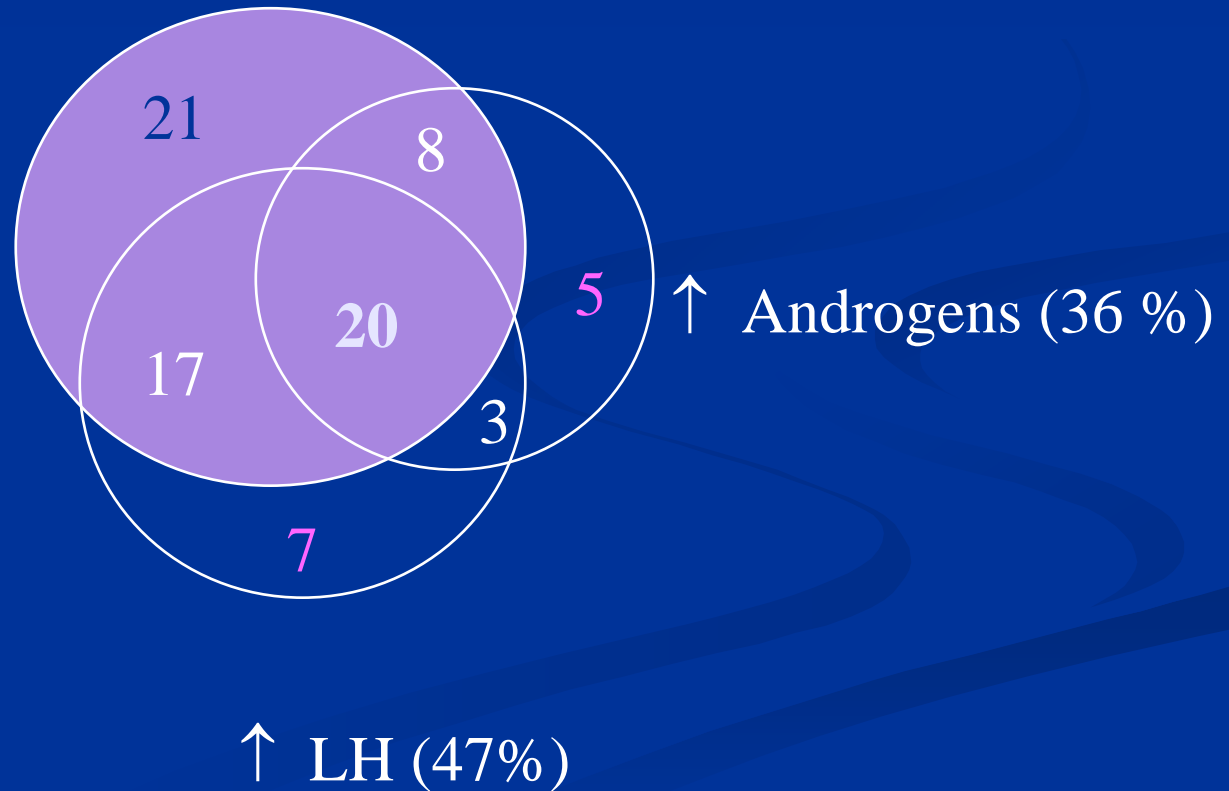
PCO

versus

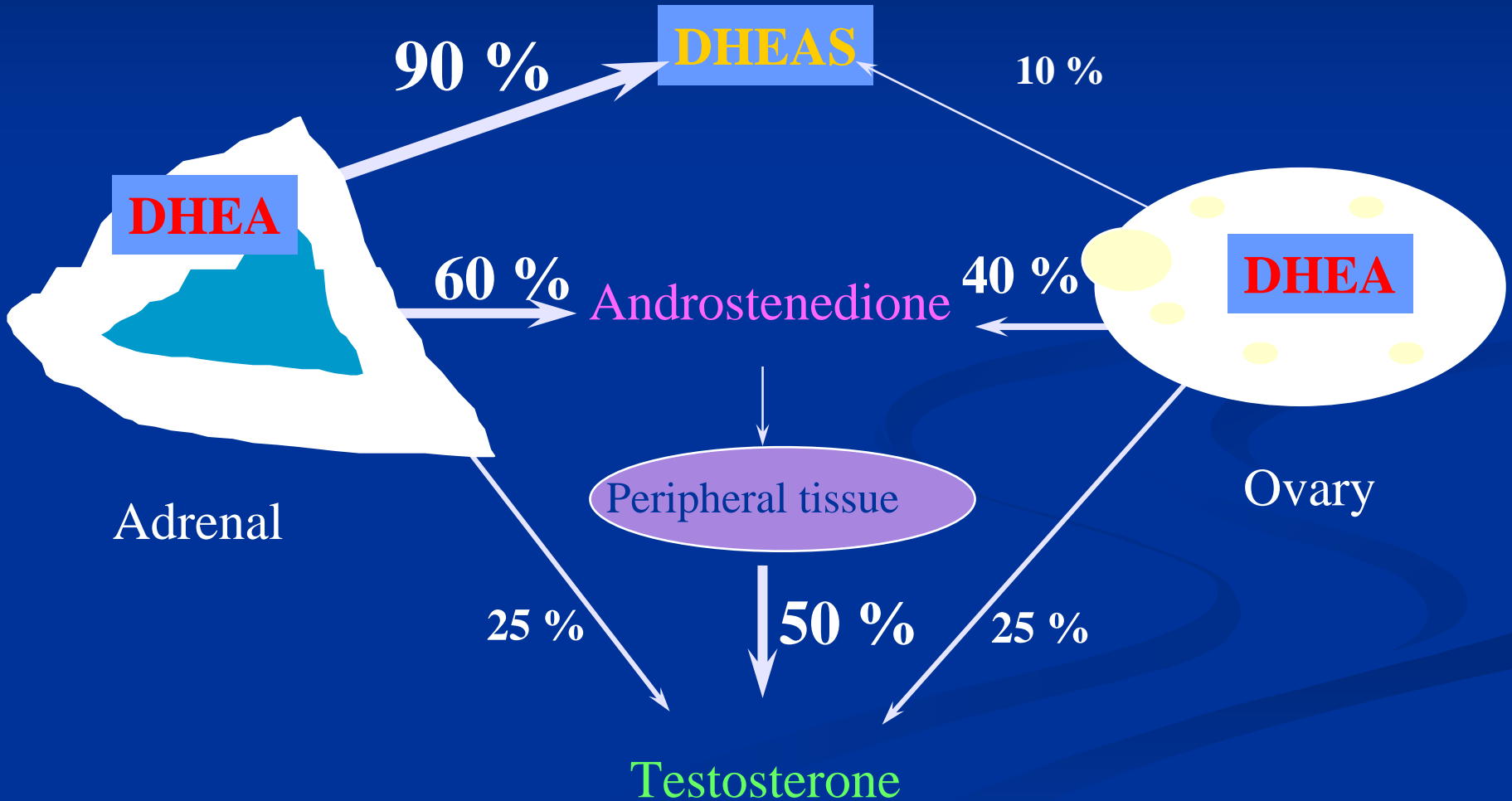
PCOS

van Santbrink et al. 1997 Fertil Steril

Ultrasound criteria (66%)



Androgens



Serum values of androgens

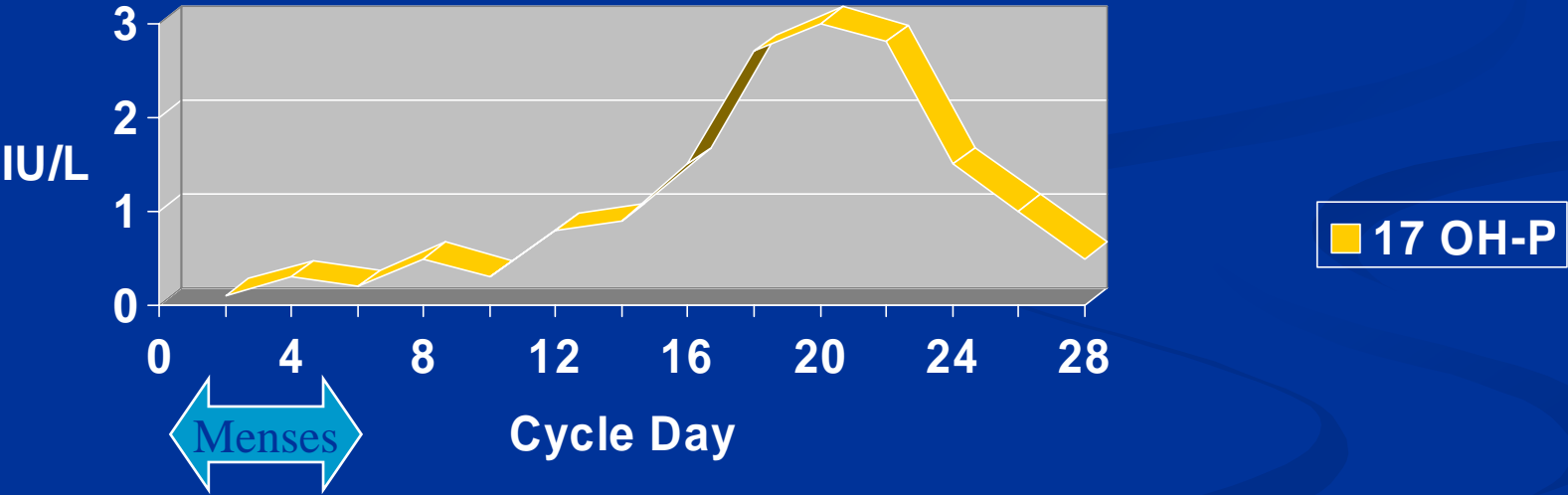
	DHEA-S ng/ml	Androstenedione ng/ml	Testosterone ng/ml
Premenopause	1600 (500 - 2800)	1.4 (0.7 - 3.1)	0.4 (0.2 - 0.8)
Menopause	800	0.8 (0.1 - 2.7)	0.15 (0.1 - 0.4)
Term pregnancy	320	2.4	4.0

Androgens and serious disease

- Testosterone
 - > 2 ng/ml
 - Look for tumor of the ovary

- DHEAS
 - > 7000 ng/ml
 - Look for tumor of the adrenal

17 OH-P and menstrual cycle



Basal values for 17 OH-P

- > 800 ng/dl (24 nmol/l)
 - 21 hydroxylase deficiency

- > 200 ng/dl (6 nmol/l)
 - Suspicion of 21 hydroxylase deficiency
 - Test with ACTH

- < 200 ng/dl (6nmol/l)
 - 21 hydroxylase deficiency

17 OH-P post ACTH

- > 1500 ng/dl
 - Late onset adrenal hyperplasia
- 1000-1500 ng/dl
 - Suspicion of late onset hyperplasia
 - Gene 21B analysis
- < 1000 ng dl
 - Heterozygote carrier

Case 3

- Cave
 - Infertility
 - Development of diabetes type 2
 - Increase in cardiovascular events ?
 - Hyperplasia and endometrial carcinoma

Case 4

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months) History of headaches and visual disturbances
- Investigations
 - Pregnancy test –
 - E₂ 28 pg/ml
 - FSH = 4 UI/L, LH 1 UI/L Prl 150 ng/ml
- Diagnosis
 - Hypogonadic amenorrhea with hyperprolactinemia

Case 4

- DD of hyperprolactinemia
 - Stress
 - Medication (neurotropes, estrogens....)
 - Hypothyroid state
 - Neurogenic (breast palpation, intercostal zona..)
 - Hypothalamic disorders
 - Pituitary disorders

Case 5

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months). History of postpartum hemorrhage with retained placenta
- Investigations
 - Pregnancy test –
 - E₂ 174 pg/ml
 - FSH = 25 UI/L, LH 58 UI/L Prl N
- Diagnosis
 - Normogonadic hypergonadotropic amenorrhea

Case 5

- Ultrasound

- $P_4 = 6,2 \text{ ng/ml}$



Case 5

- Hysterosalpingography



- Hysteroscopy



Case 6

- 25 years old athlete with secondary amenorrhea after stopping OC (> 12 months). History of postpartum hemorrhage with retained placenta. She could not breastfeed.
- Investigations
 - Pregnancy test –
 - E₂ 10 pg/ml
 - FSH = 1 UI/L, LH 0.2 UI/L Prl 4 ng/mL
- Diagnosis
 - Hypogonadic hypogonadotropic amenorrhea

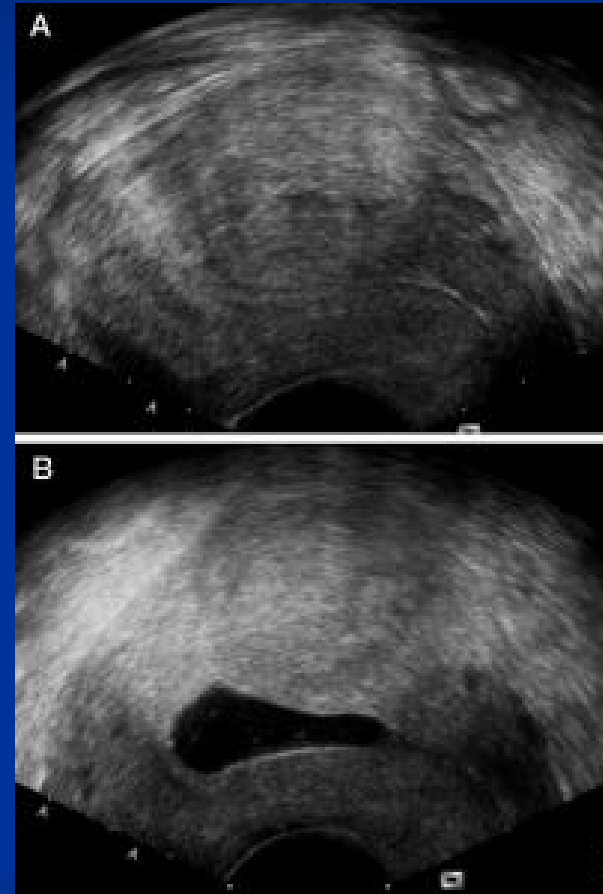
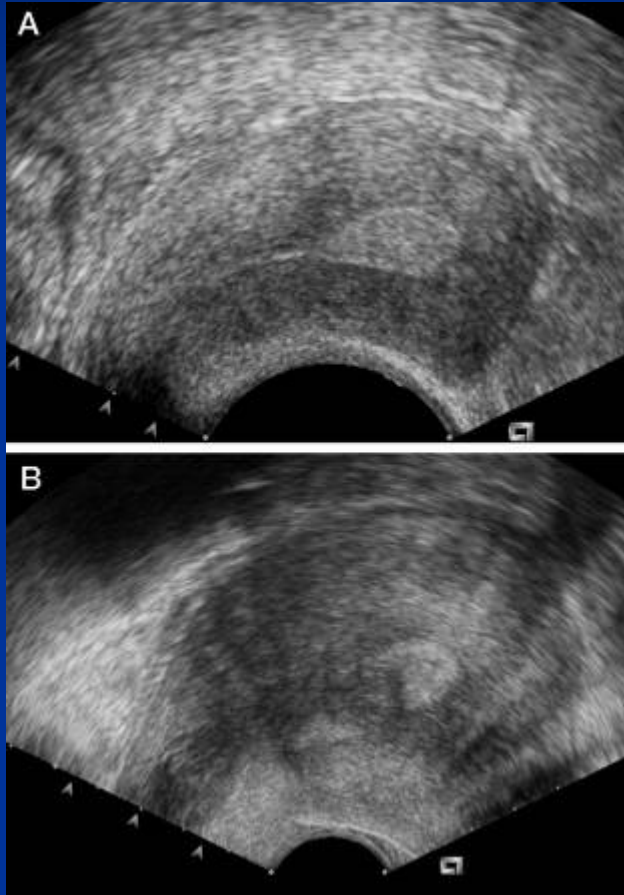
Case 6

- Sheehan Syndrome
- Test the endocrine axis
- CNS MRI
- Hormonal substitution according to the endocrine deficits

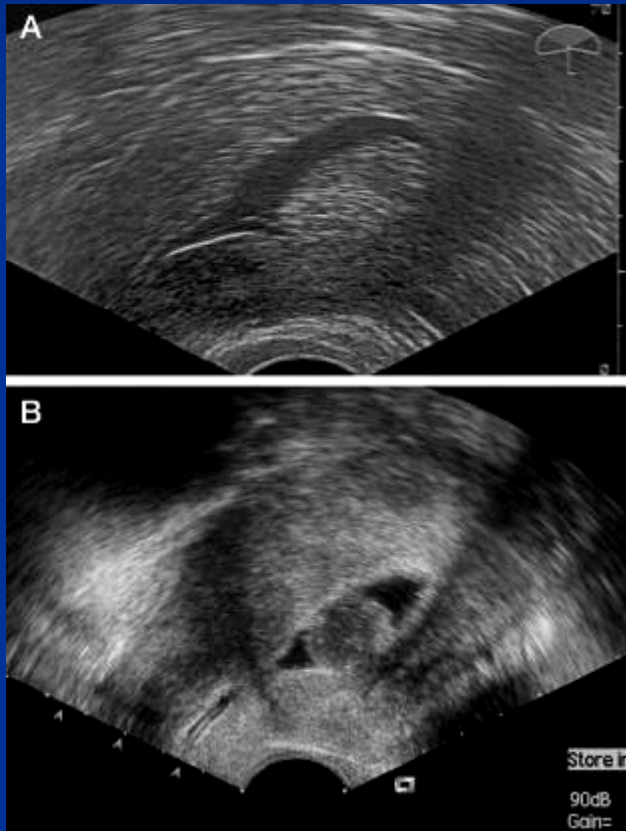
Case 7

- 42 year old lady complaining of menorrhagia and secondary dysmenorrhea since 2 years
 - Normal pelvic examination
 - PAP smear normal

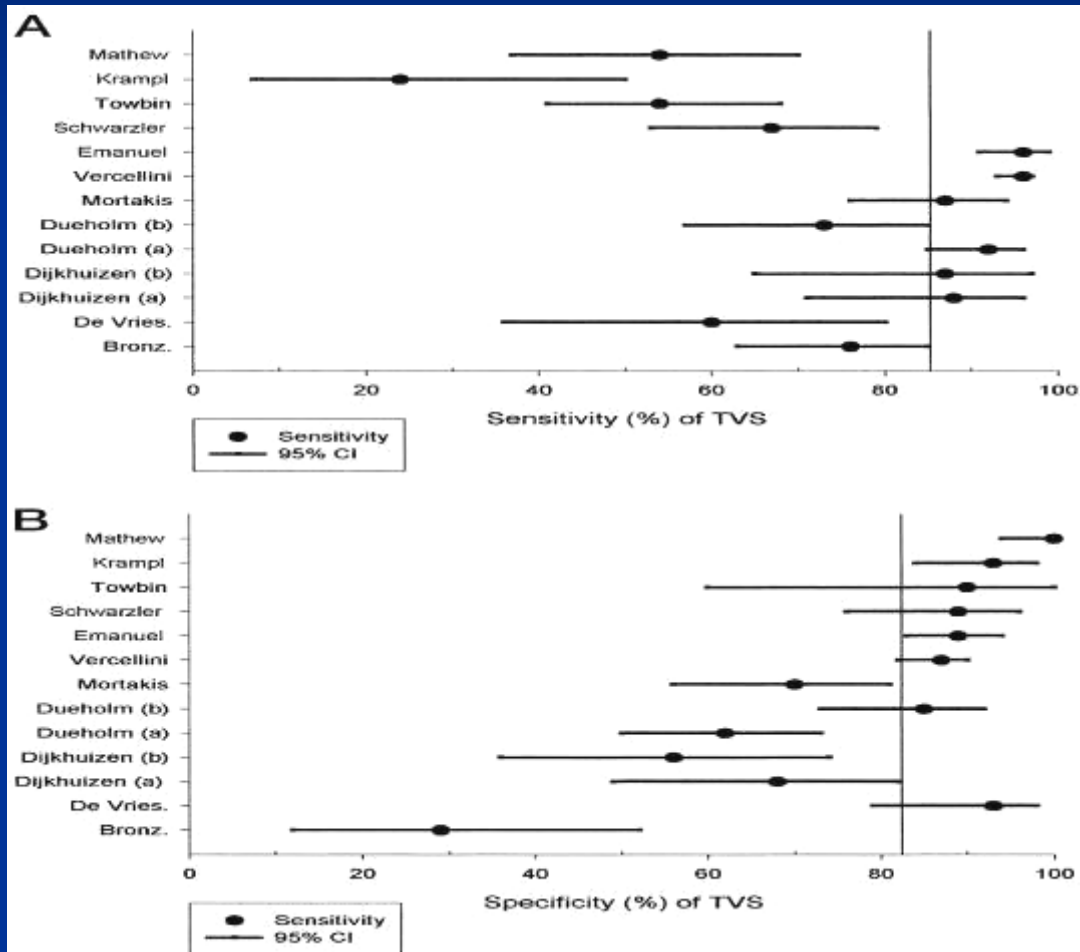
TVS and HTVS



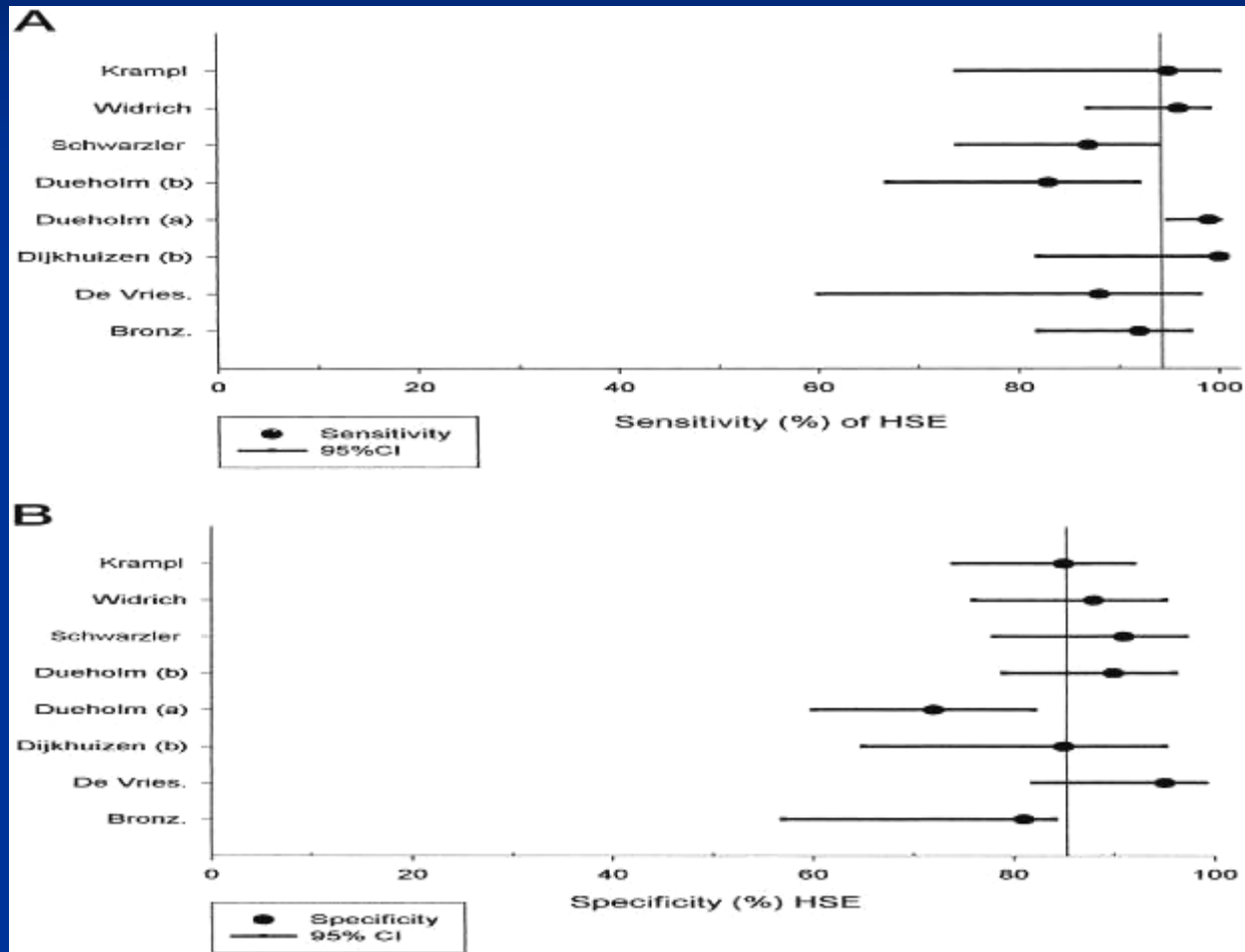
HTVS vs hysteroscopy



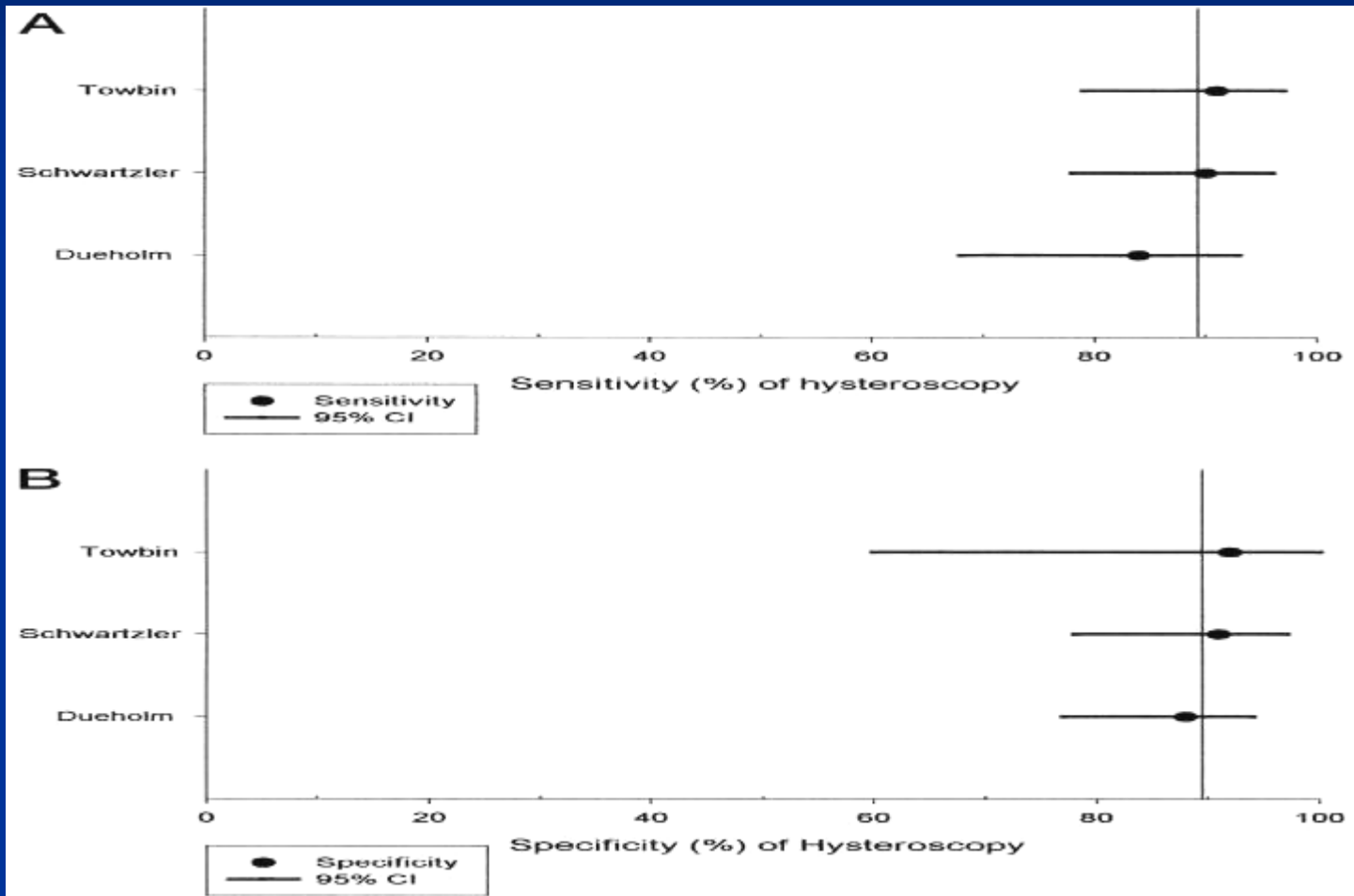
TVS



HTVS



Hysteroscopy



Case 8

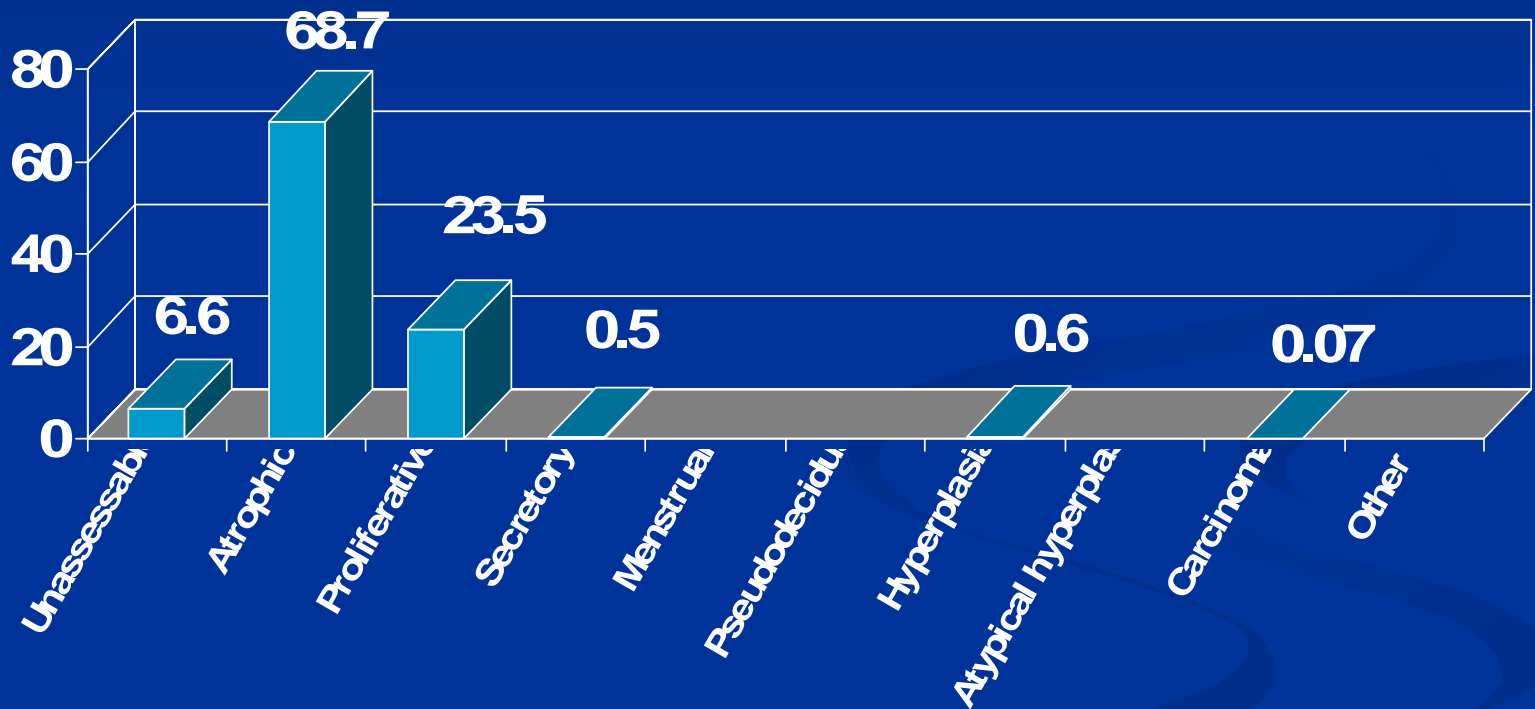
- 59 year old women on sequential HRT complaining of metrorrhagia during the progestational phase
 - Normal pevic examination
 - PAP smear normal

Case 8

- TVS: endometrium of 4.5 mm no uterine pathology

Endometrial histology without HRT

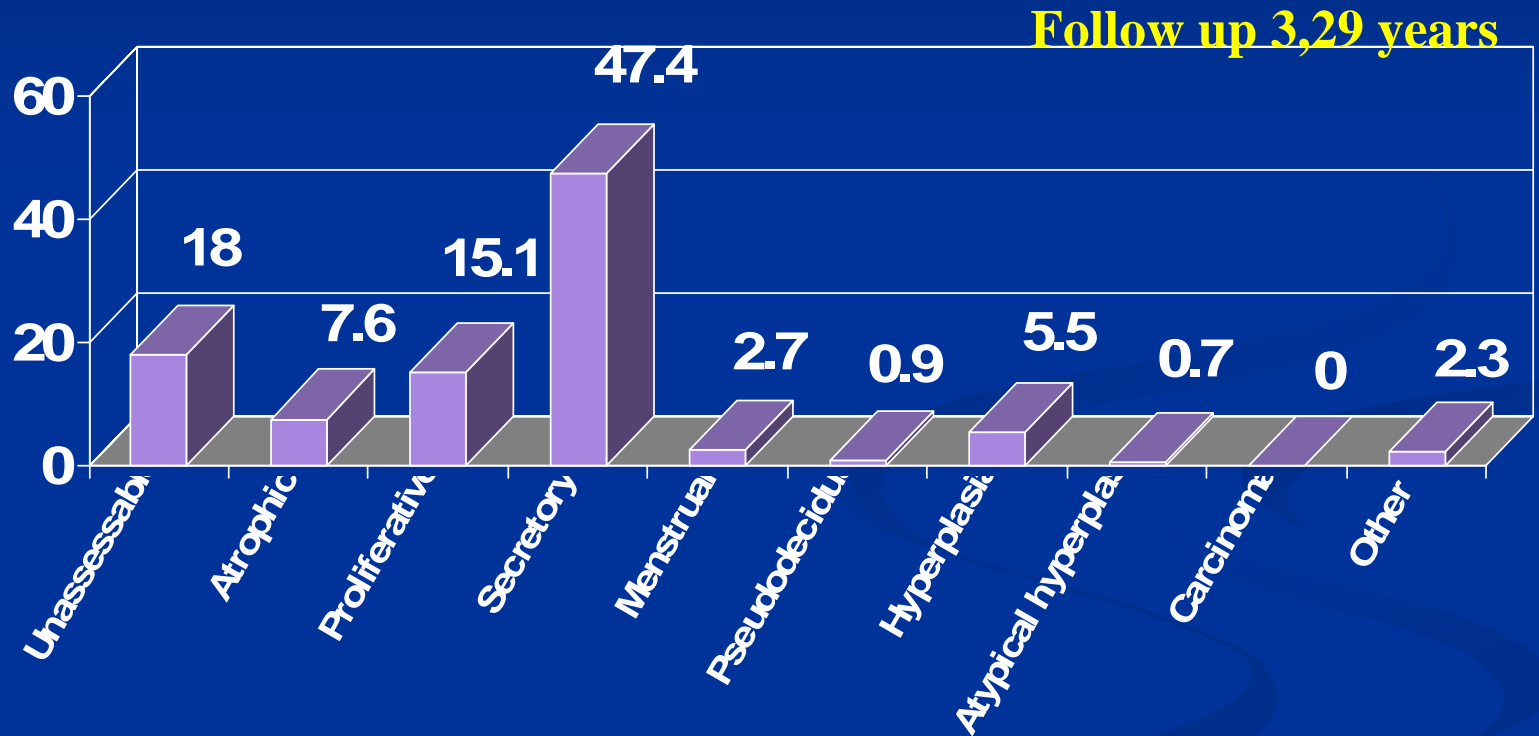
Korhonen et al. CHART 2 1997 AJOG



n= 2964

Endometrial histology with sequential HRT

Sturdee et al. 2000 BJOG

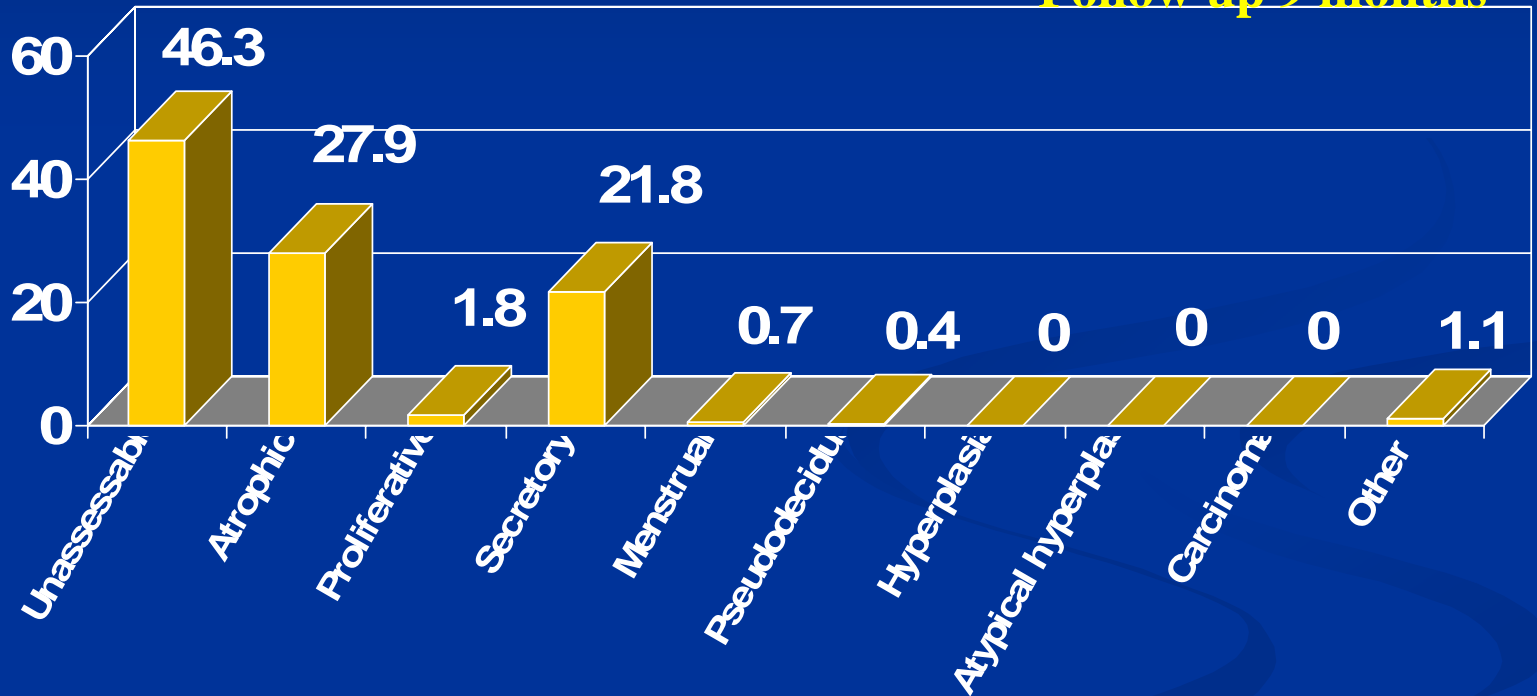


n=1192

Endometrial histology with continuous HRT

Sturdee et al. 2000 BJOG

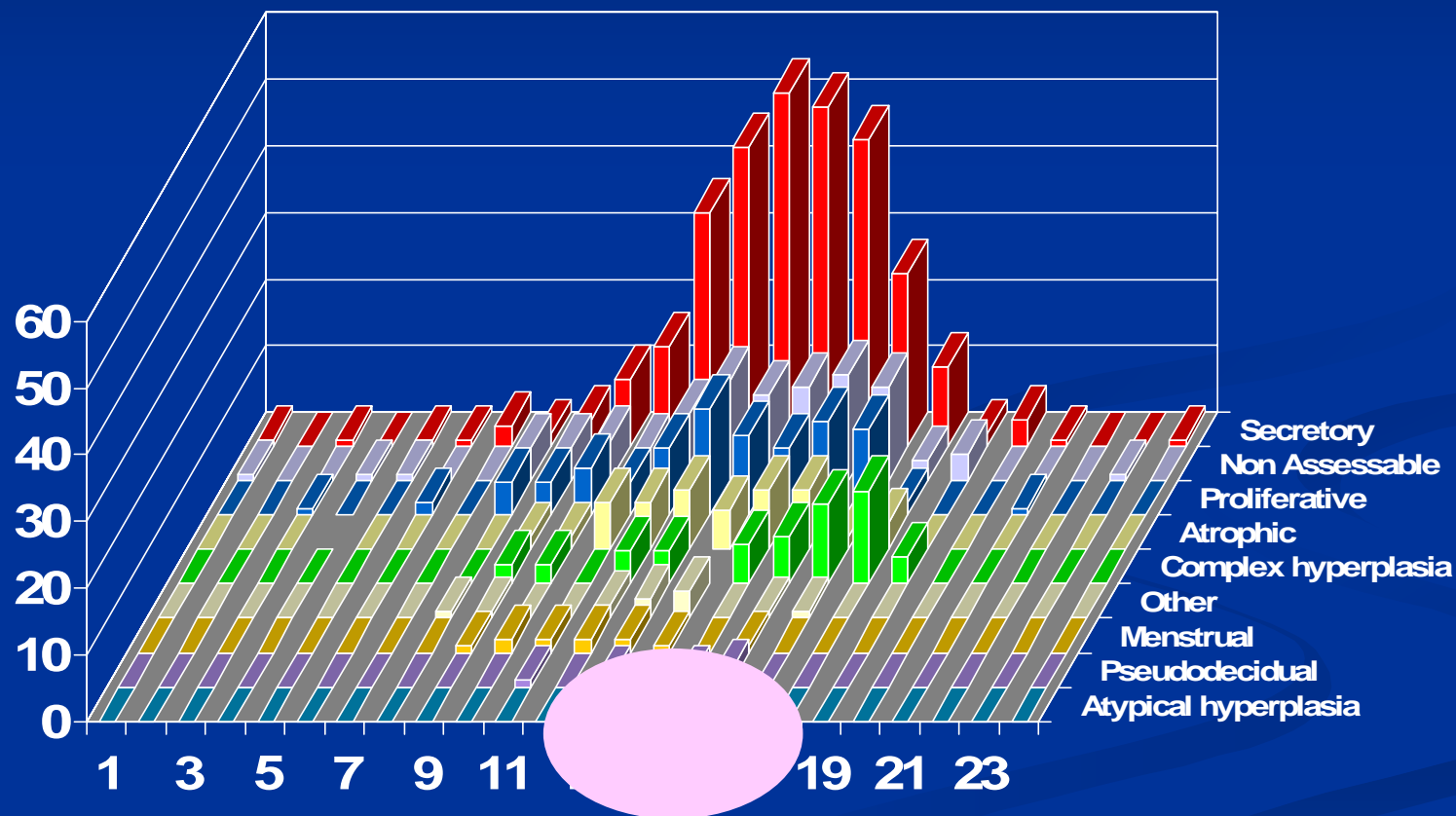
Follow up 9 months



n=1196

First bleeding day from the start of progestogen phase in sequential HRT and endometrium histology

Sturdee et al. 1994 Lancet



Endometrial thickness in postmenopausal women

Andolf et al. Obstet and Gynecol 1993

Endometrial thickness	> 5mm	< 5 mm	P
E ₁ (pmol/L)	219 _± 20	175 _± 35	0.01
E ₂ (pmol/L)	38 _± 17	13 _± 2.7	0.05
P ₄ (nmol/L)	1 _± 0.2	0.87 _± 0.05	
BMI	29.1 _± 1.2	25.6 _± 0.3	0.02

Endometrial thickness in sequential therapy *Gull et al.*

Cycle day	Endometrial thickness (mm)	N
1-7	4.3 \pm 1.0	4
8-14	6.8 \pm 1.2	13
15-21	6.0 \pm 0.3	11
22-28	6.2 \pm 0.6	14

Vaginal sonography and endometrial cancer

Buyuk et al. 1999 Acta Obstet Gynecol Scand

- 54 with spontaneous postmenopausal bleeding
 - Atrophy 5 mm
 - Hyperplasia 8.6 mm
 - Cancer 6 mm

- *Out of 9 cancers 3 had an endometrial thickness of 3mm*