

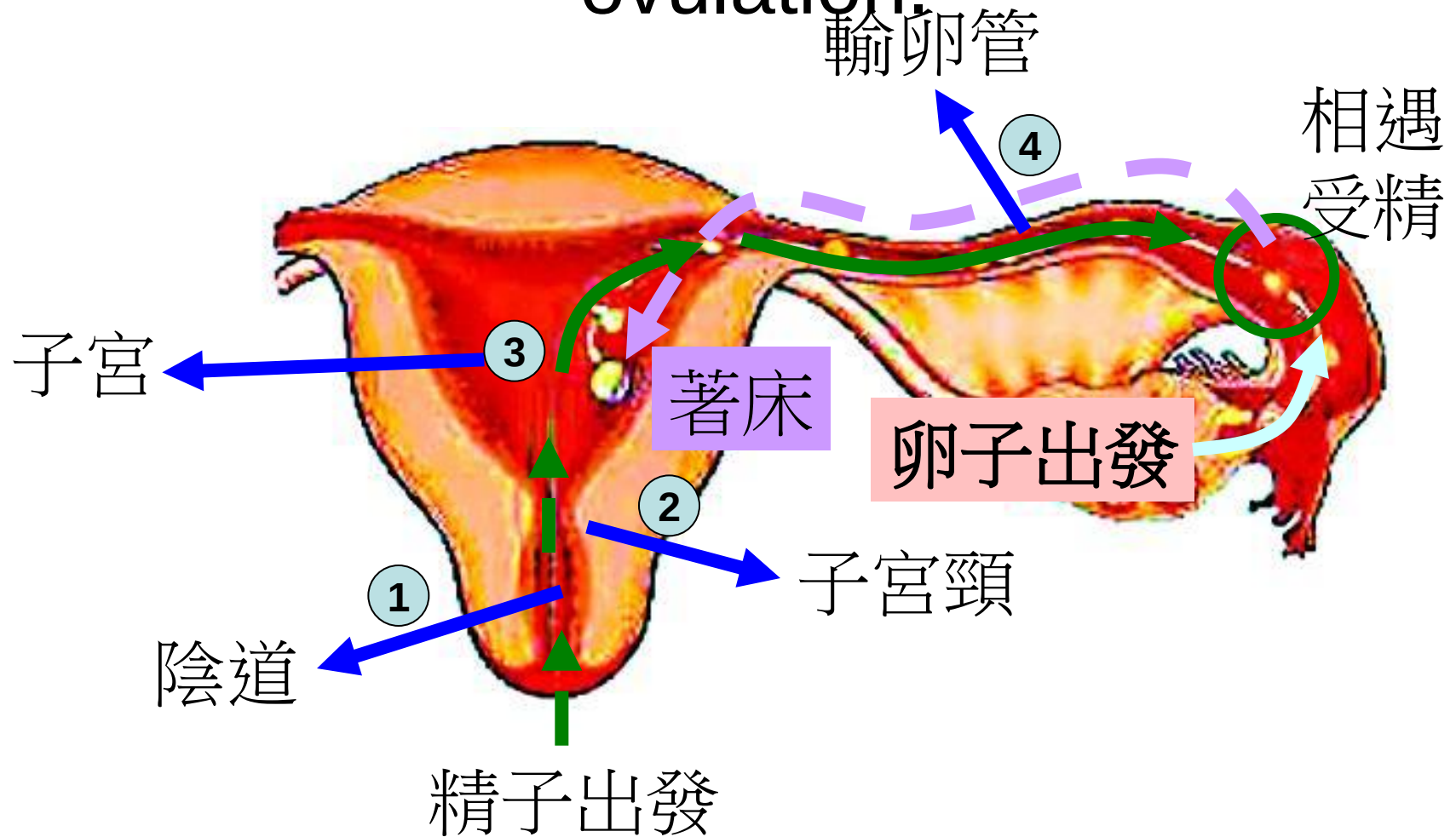
～主治醫師教學～ 不孕症治療

黃貞瑜醫師

台北榮民總醫院
婦產部



The high-possibility fertile phase extends from 5 days before ovulation to the day of ovulation.



spermatozoa can survive in the female reproductive tract for 5–6 days after intercourse

Semen Analysis

Criteria	4th ed	5th ed
Volume	≥ 2.0 mL	≥ 1.5 mL
Total sperm number	≥ 40 millions/ejaculate	≥ 39 millions/ejaculate
Sperm concentration	≥ 20 millions/ mL	≥ 15 millions/ mL
Total motility	$\geq 50\%$	$\geq 40\%$
Progressive motility	$\geq 25\%$	$\geq 32\%$
Normal morphology	$\geq 15\%$	$\geq 4\%$ (Kruger Strict criteria)
Vitality	$\geq 50\%$	$\geq 58\%$
pH	>7.2	>7.2

Liquefaction: Complete within 60 minutes at room temperature

Appearance: Homogeneous, gray, and opalescent

Consistency: Leaves pipette as discrete droplets

Leukocytes: Fewer than 1 million/mL

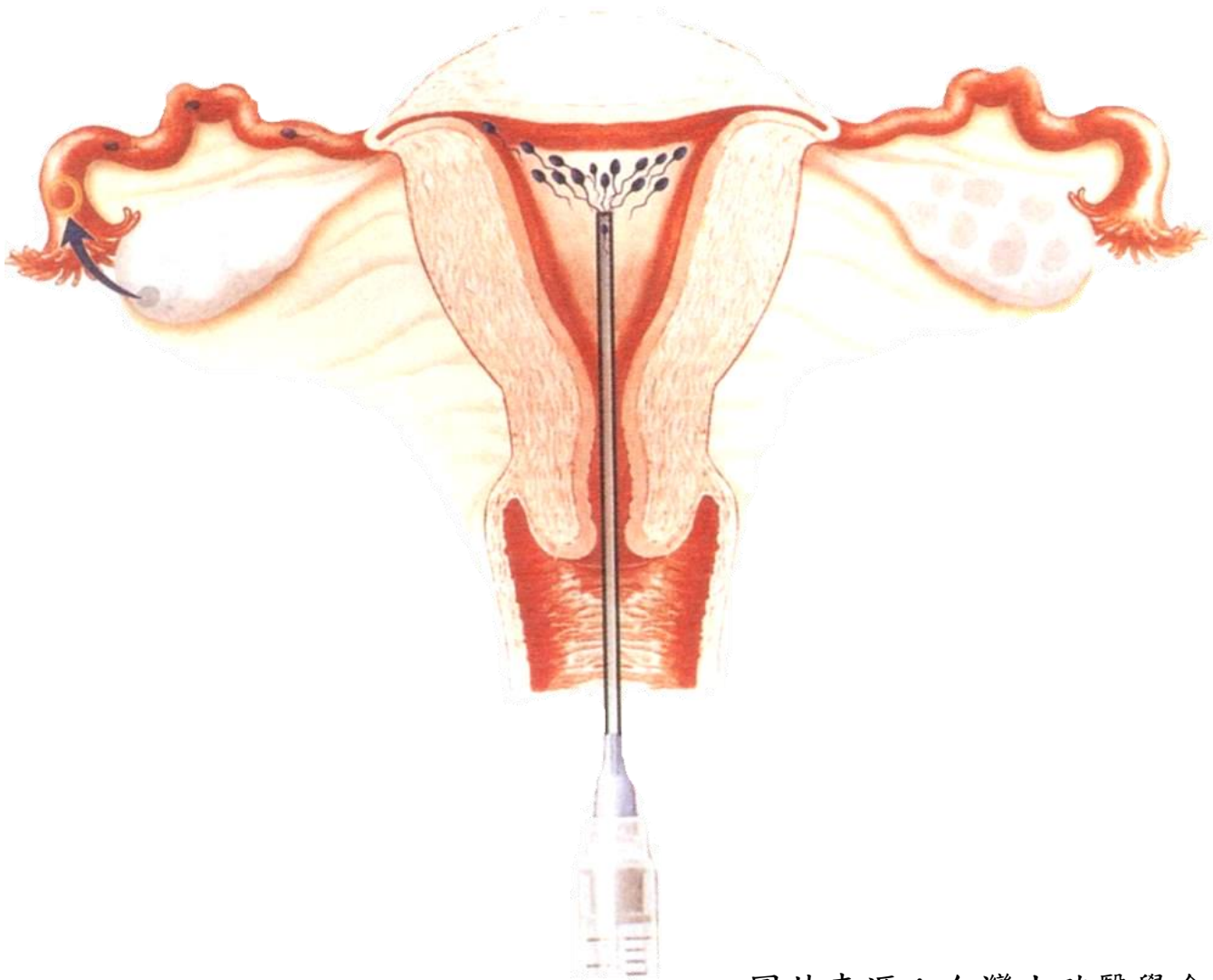
Assisted Reproductive Techniques

- Intra-Uterine Insemination (IUI)
 - Artificial Insemination with Husband (AIH)
 - Artificial Insemination with Donor (AID)
- Gamete intra-fallopian transfer (GIFT)
- Zygote intra-fallopian transfer (ZIFT)
- *In vitro* fertilization (IVF)
- Intracytoplasmic sperm injection (ICSI)
- Pre-implantation genetic diagnosis (PGD)

IUI, 配偶人工授孕(AIH)

- ✱（一）適應症：男性精蟲稀少（**每西西一千萬左右**），尿道下裂、陰莖畸型、陽萎、早洩、女性陰道痙攣不能性交、配偶常出差等。
- ✱（二）方法：男性將精液取出，經液化後，將精蟲洗滌，去除精液之雜質，在女性排卵期將精液注入子宮腔。

Intra-Uterine Insemination

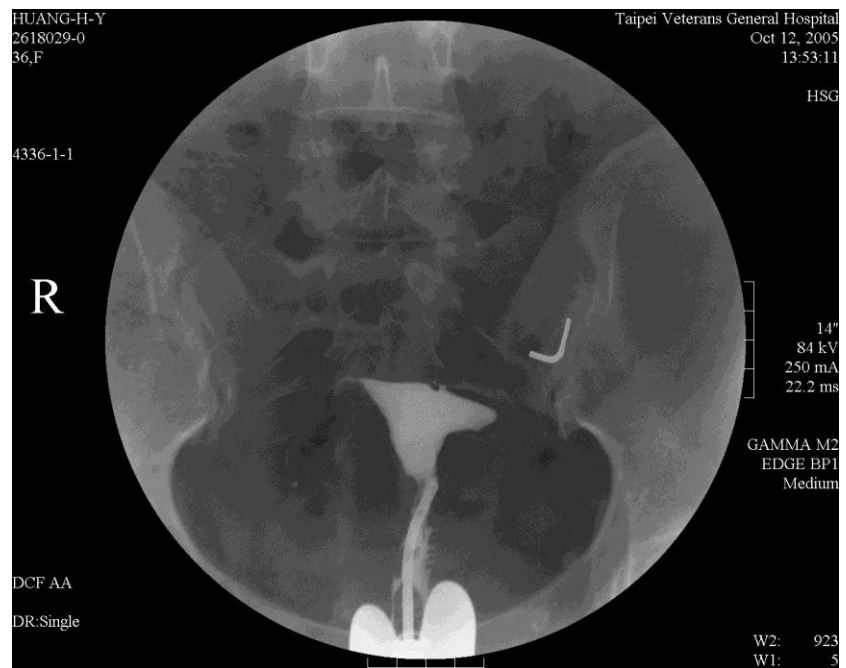


圖片來源：台灣生殖醫學會網站

Male Factor Infertility

- Best results with IUI are achieved when Total motile sperm count (TMC) in the insemination specimen **exceeds 10 million** **14% or more have normal morphology**
- Higher counts do not increase success
- IUI is **seldom successful if fewer than 1 million** total motile sperm are present

黃玉

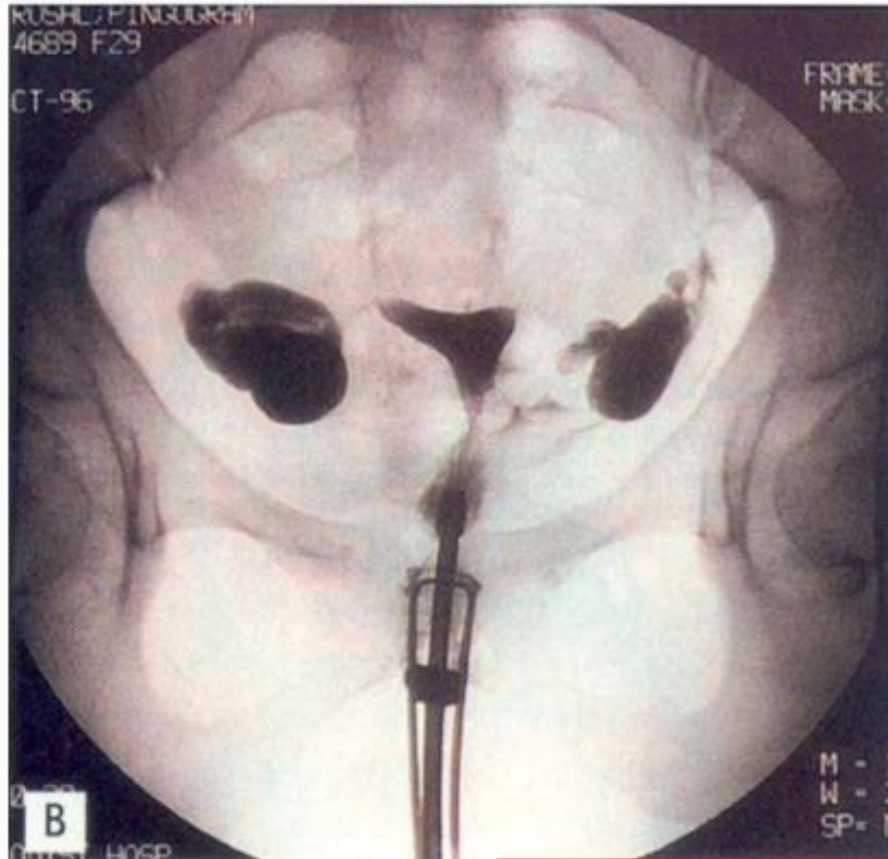


陳貞



102年第一次醫師(二)醫學(六)

- 54 一位 32 歲女性，結婚多年未懷孕，主訴無任何系統性疾病，子宮輸卵管攝影如下圖。雙側輸卵管水腫大於 4 公分，下列處置，何者懷孕機會較高？



- (A) 接受輸卵管修補手術
(B) 接受輸卵管切除後做 IVF (*in vitro* fertilization)
(C) 直接施行 IVF (*in vitro* fertilization)
(D) 直接施行 IUI (intrauterine insemination)

Male Factor Infertility

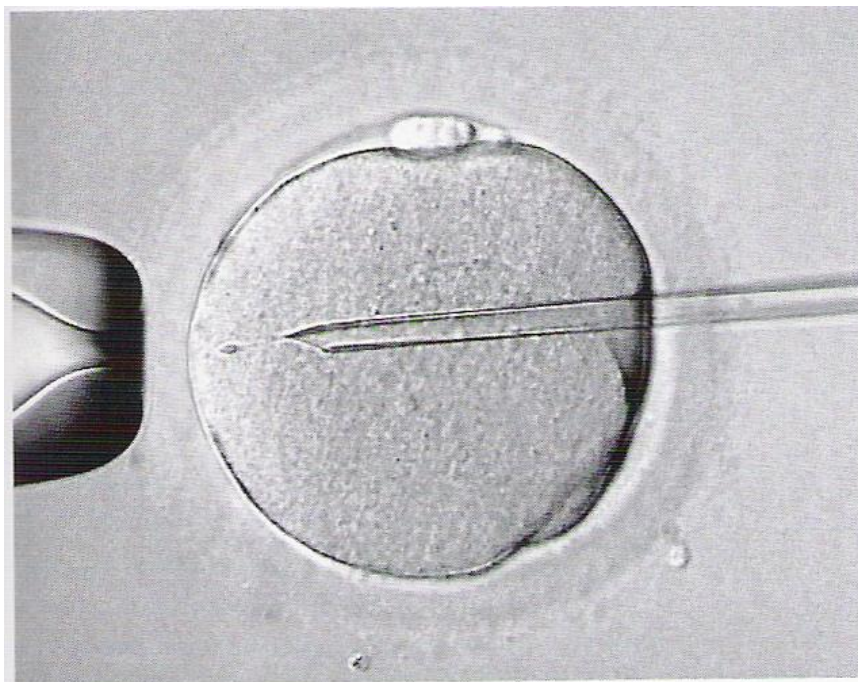
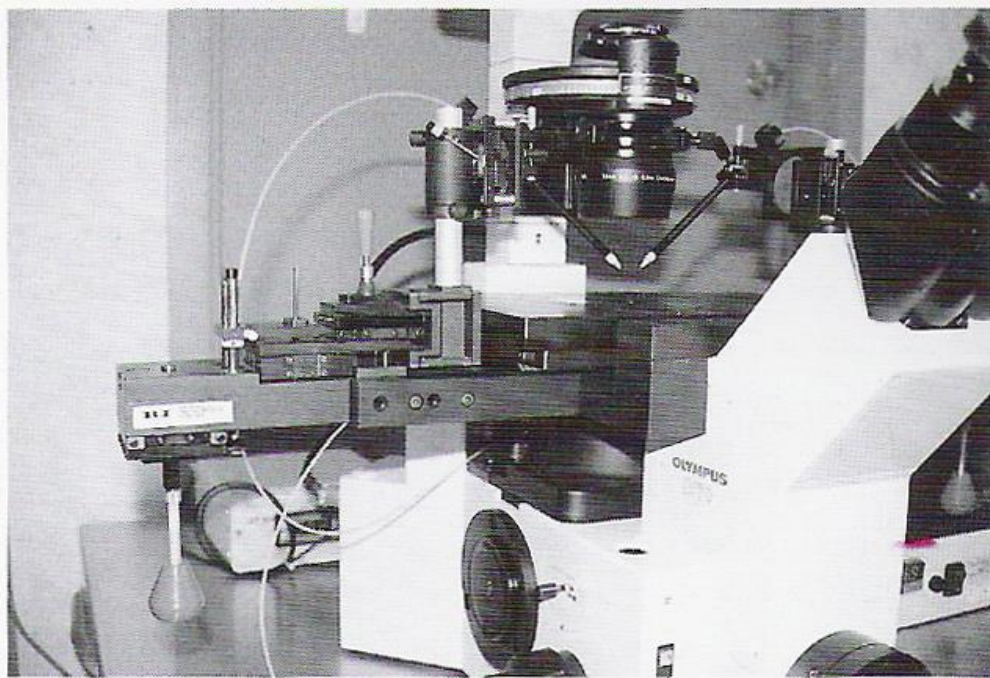
- TMC < 1 million: ICSI
- TMC > 1 and < 10 million:
IVF can be performed if infertility duration is 2 years or longer
- TMC > 10 million: IVF is indicated if the duration is 3 years or longer. If the woman is older than 36 years, IVF may be considered earlier

體外授精（試管嬰兒）IVF

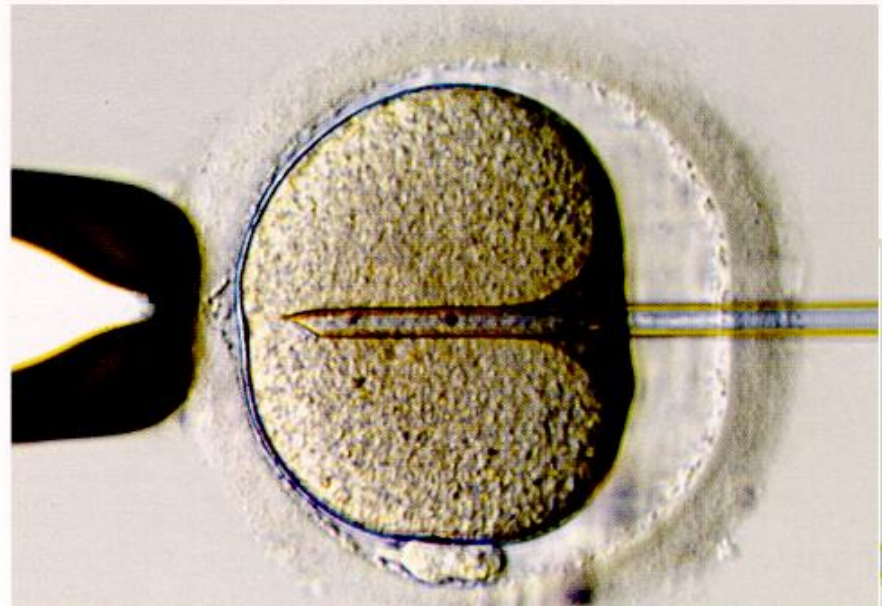
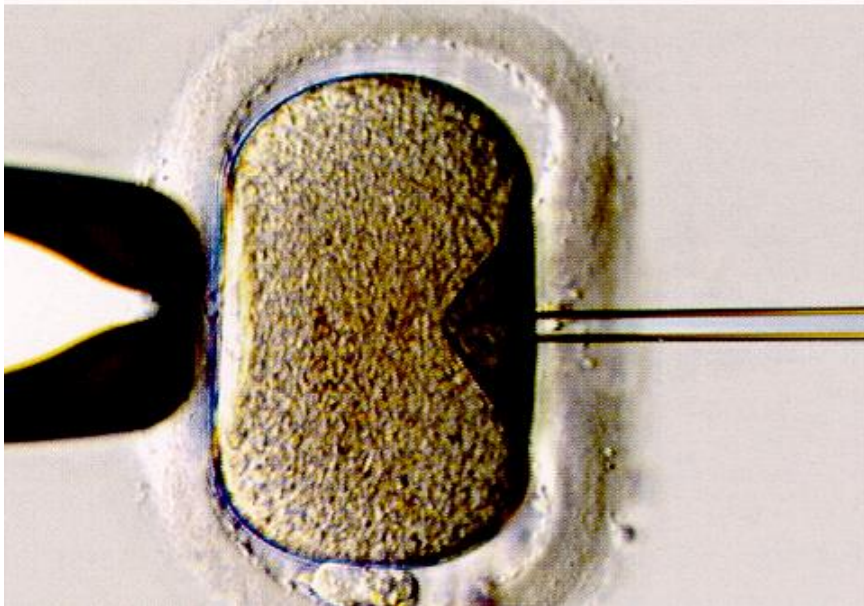
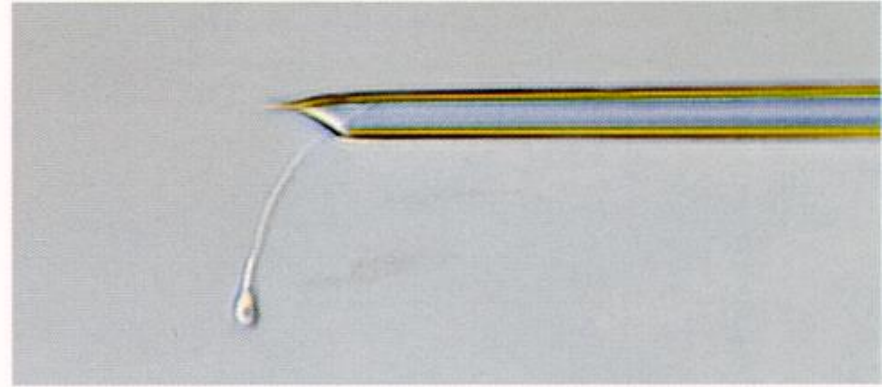
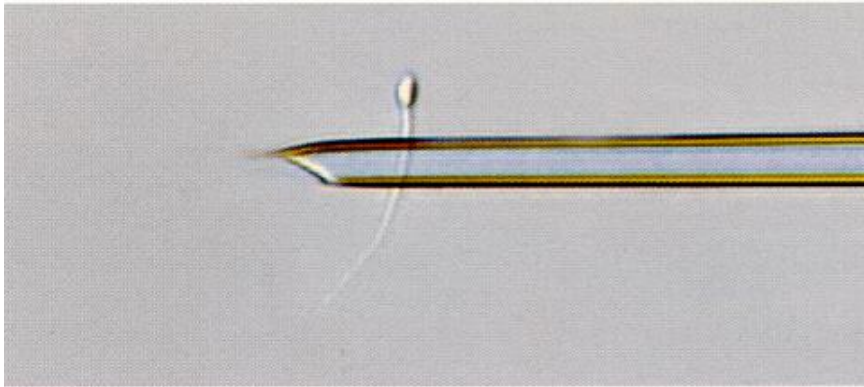
- ✱（一）適應症：骨盆腔粘連、輸卵管堵塞、輸卵管切除、嚴重度子宮內膜異位、精子稀少（五百萬左右）、精蟲產生抗體等。
- ✱（二）方法：
- ✱(1)用排卵物誘導排卵
- (2)利用超音波檢查卵泡及抽血測E2
- (3)當卵子成熟，利用陰道超音波，將卵子取出
- (4)在實驗室將精子與卵子完成受精分裂成胚胎，再植入子宮腔

精蟲顯微注射：(ICSI)

應用在合併男性不孕或先前嘗試受精率低者



IntraCyttoplasmic Sperm Injection



Male Factor Infertility

- **Indications for ICSI**

Total motile sperm count < 1 million
< 4% normal morphology and TMC < 5 million

No or poor fertilization in the first IVF cycle when TMC < 10 million

No or poor fertilization in two IVF cycles when TMC > 10 million

Epididymal or testicular spermatozoa

精卵顯微授精法（microinjection）

（一）適應症：

- (1)嚴重精蟲稀少（在一百萬隻左右）、精蟲活動力差、IVF不能受精者。
- (2)精液檢查無精子，但睪丸組織有精子，請泌尿外科大夫，將精子吸出在實驗室處理。

*（二）方法：

在顯微鏡下，將一隻精子注射入卵子，因注射部位不同，可分為

(A)透明層下注射法(sub-zonal injection; suzi)

(B)透明層開洞方法(partial zonal dissection; PZD)

(C)精子注射入卵細胞漿法(intracytoplasmic sperm injection ICSI)，因ICSI方法受精機率高，且懷孕成功機率也高，目前廣為世界採用。

93 年第2次專技高考外科學(二)

B 男性不孕患者，精液檢查總活動數精蟲少於 1 百萬，實施人工協助生殖技術時，下列何項處置最為有效？

- A. 透明區穿孔術（zona drilling）
- B. 卵質內單一精蟲注入術（intracytoplasmic sperm injection）
- C. 透明區下精蟲注入（subzonal sperm injection）
- D. 透明區磨薄術（assisted hatching）

102年第二次專技醫師二醫學六

- C** 一位26歲男性，不孕3年求診，嚴格的精液分析顯示：精液量 = 2.5 mL，總精蟲數 = $1 \times 10^6/\text{mL}$ ，4%直線前進，3%正常外觀精子，下列處理何者較適當？
- A. 進行子宮腔內受精（intrauterine insemination）
 - B. 進行體外受精（in vitro fertilization）
 - C. 進行卵質內單一精子注入（intracytoplasmic sperm injection）
 - D. 進行睪丸切片取精（testicular sperm extraction）

* 一對夫妻到門診作不孕症檢查，妻子 30 歲，月經週期正常，週期第 3 天 FSH 7.2 IU/L，雙側輸卵管通暢，先生的精蟲數目為 20 萬/mL，活動力 10%，先生的染色體為 46XY，無 Y chromosome microdeletion。你會建議他們作何治療？

- A. 人工受精（intrauterine insemination; IUI）
- B. 傳統試管嬰兒（in vitro fertilization; IVF）
- C. 細胞內精蟲顯微注射（intracytoplasmic sperm injection; ICSI）
- D. 禮物嬰兒（gamete intrafallopian transfer; GIFT）

C

B 男性不孕患者，精液檢查總活動數精蟲少於1 百萬，實施人工協助生殖技術時，下列何項處置最為有效？

A 透明區穿孔術（zona drilling）

B 卵質內單一精蟲注入術（intracytoplasmic sperm injection）

C 透明區下精蟲注入（subzonal sperm injection）

D 透明區磨薄術（assisted hatching）

A 關於不孕症的敘述，何者錯誤？

A 做細胞內精蟲顯微注射（intracytoplasmic sperm injection, ICSI）的懷孕率比傳統試管嬰兒（*in vitro* fertilization, IVF）的懷孕率低

B 不孕症是指在未避孕的情況下，一年以上沒有懷孕

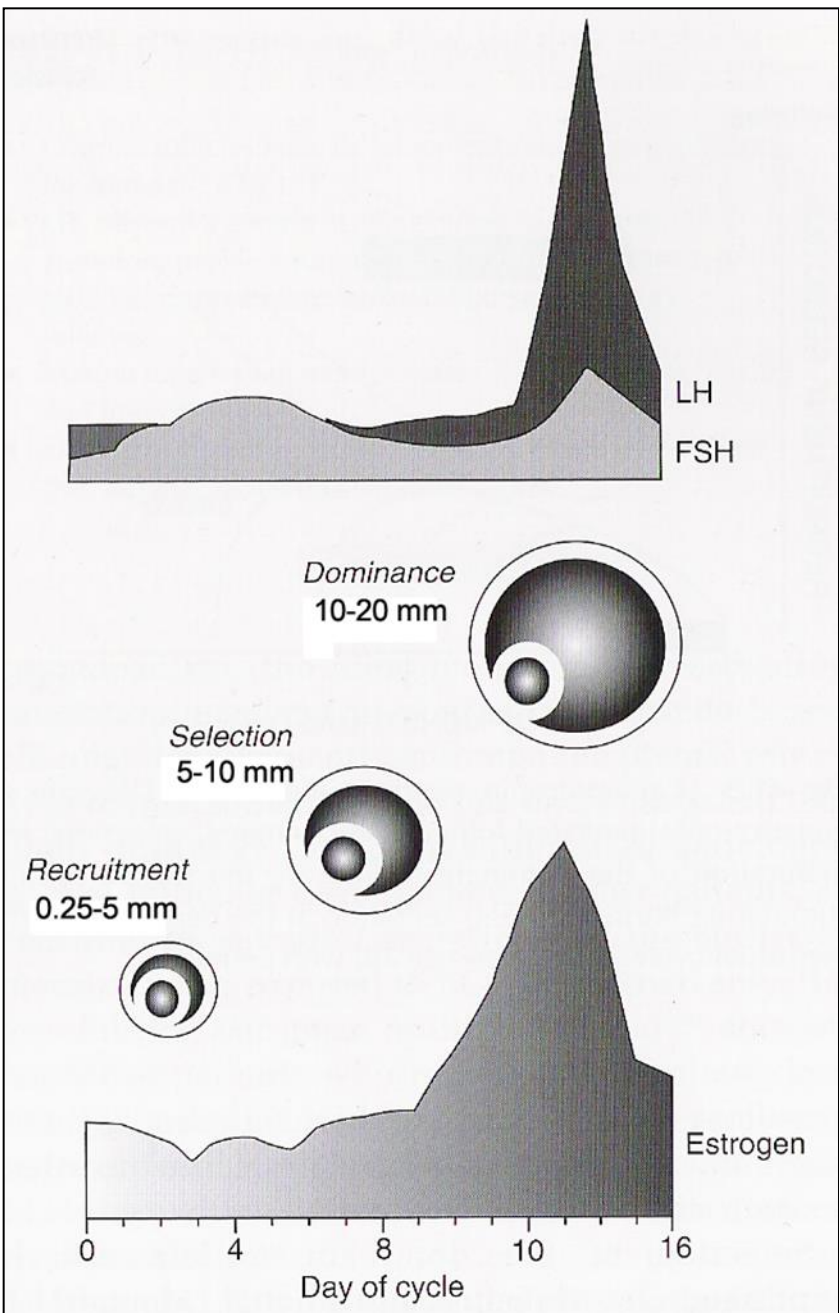
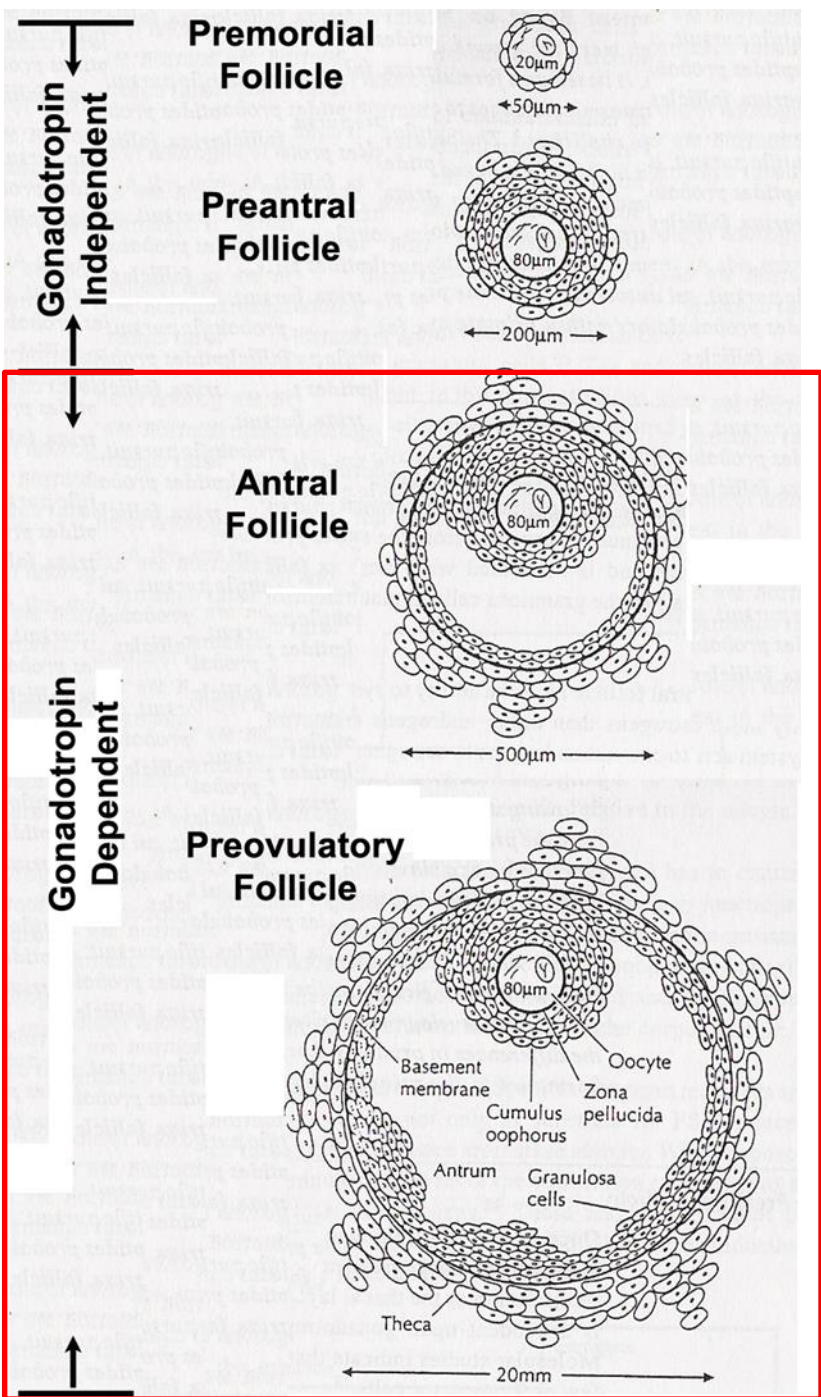
C 所謂人工生殖技術（assisted reproductive technology, ART）是指各種取卵的介入方法

D 女性的懷孕能力（fecundability）從30歲後開始下降

濾泡發育與誘導排卵

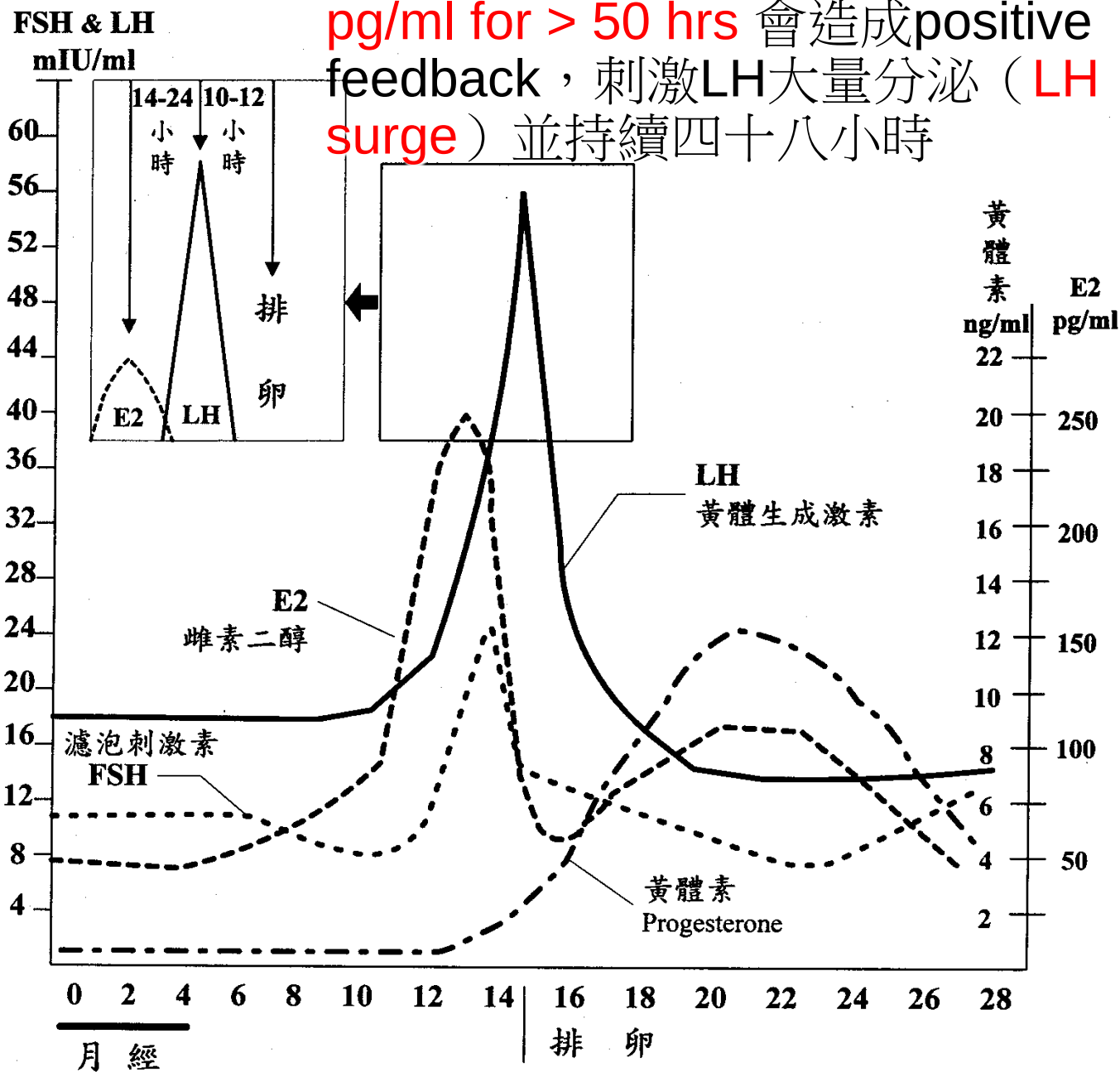
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婦產部





* 一個 dominant follicle → E2 > 200 pg/ml for > 50 hrs 會造成 positive feedback, 刺激 LH 大量分泌 (LH surge) 並持續四十八小時

圖3 正常月經週期內荷爾蒙的變化



雌激素

稍許上升

大幅上升

(50-150 pg/ml)

> 200 pg/ml
超過50小時

負性迴饋

抑制濾泡刺激素

正性迴饋

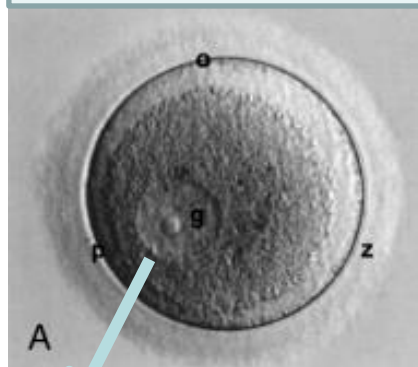
增加黃體刺激素

月經

排卵

Oocytes

Before LH surge



Germinal Vesicle (GV)–intact

Meiotic Arrest at Diplotene, Prophase of Meiosis I

14–24 hours

10–12 hours

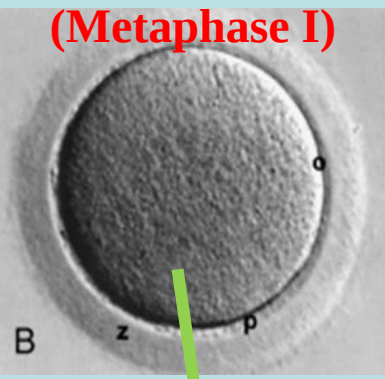
OVULATION

LH

LH刺激卵子成熟

Meiotic Resumption (→ M II)
just before ovulation

(Metaphase I)

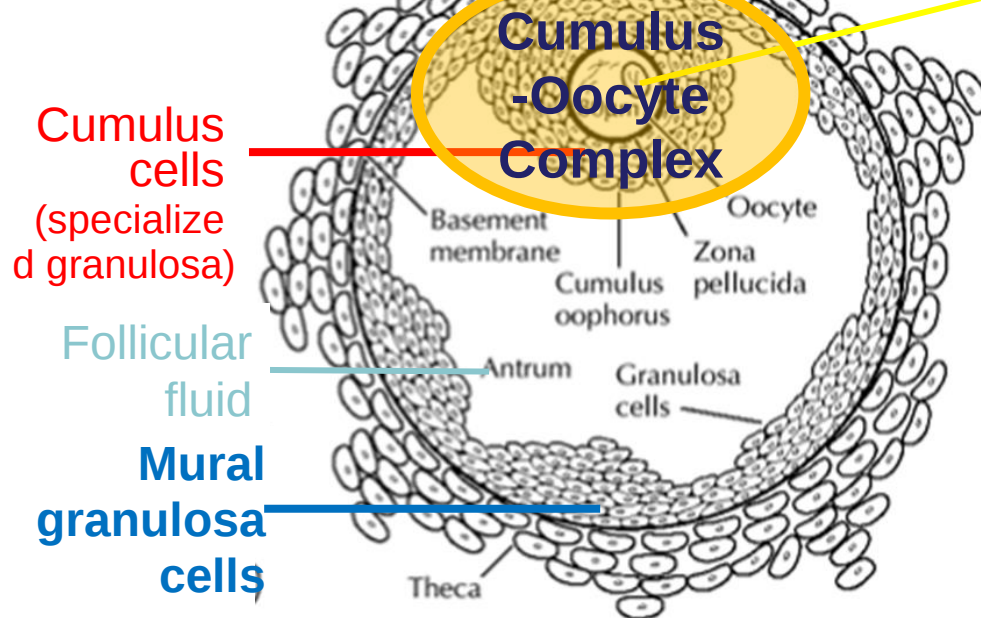


GV breakdown (GVBD)
= Meiosis I resumes

(Metaphase II)

Meiotic Arrest at Metaphase of Meiosis II

Pre-ovulatory follicle
= Graafian follicle



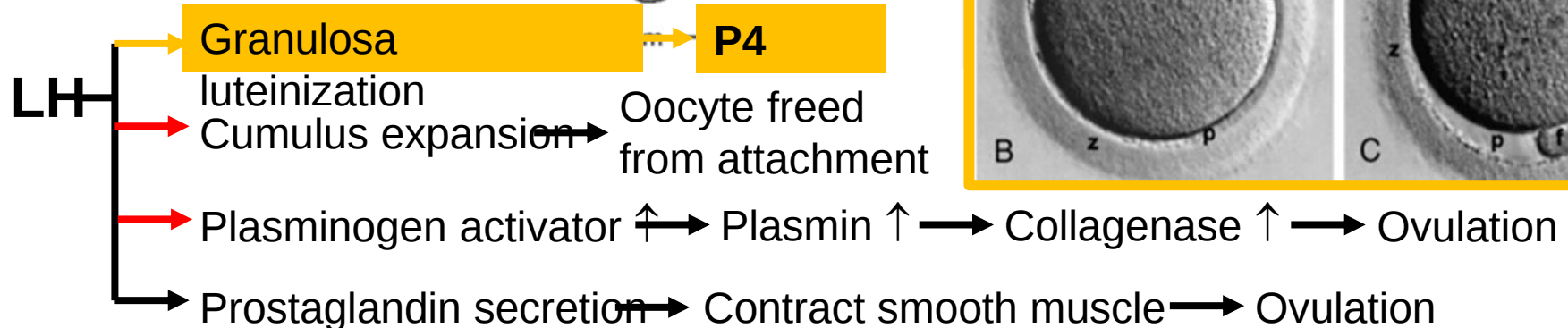
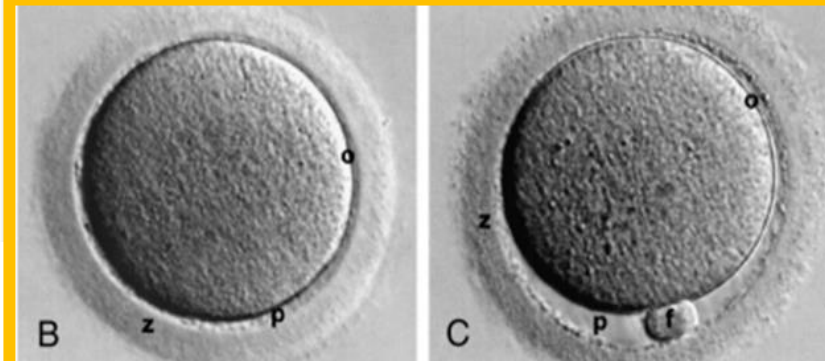
Oocyte
(GV intact)

A

LH surge

LH刺激卵子成熟

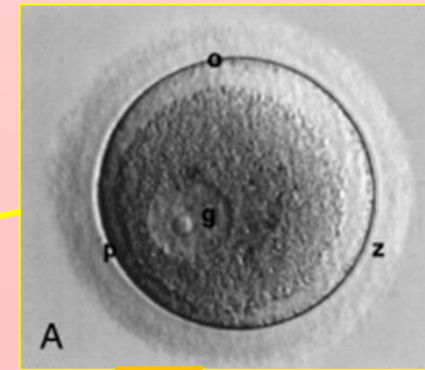
Meiotic Resumption (→ M II)



LH(或人工生殖中取代LH的hCG) 之四大功能

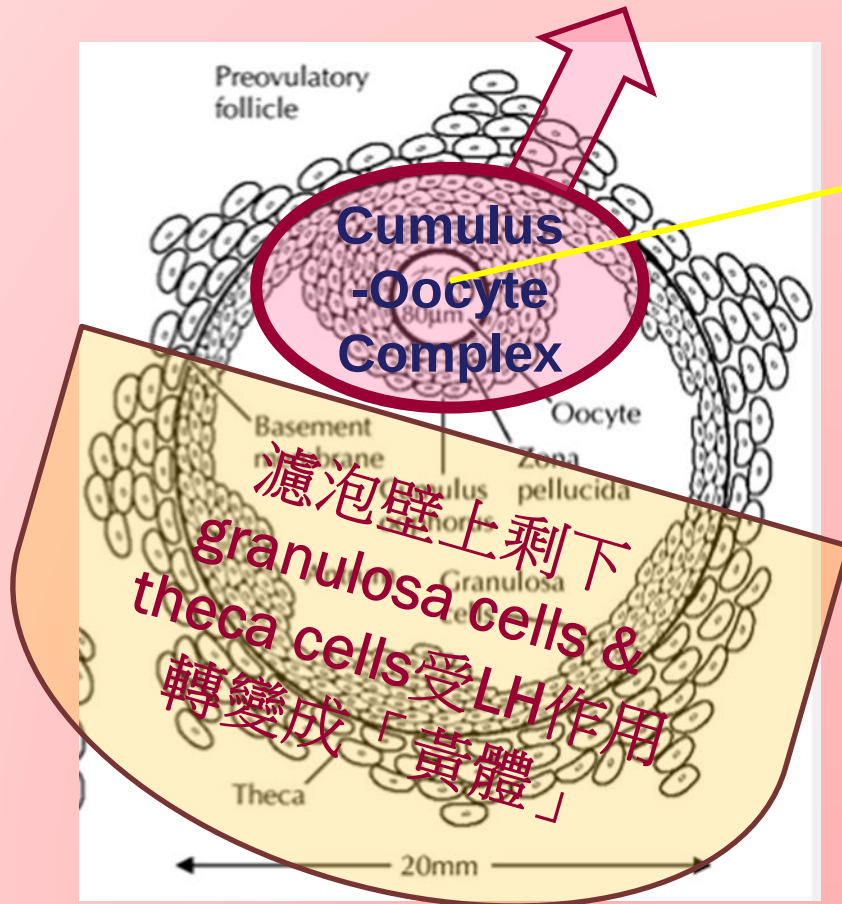
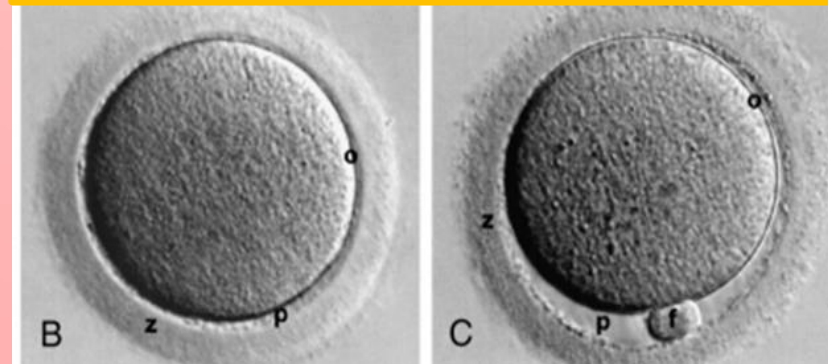
1. 讓卵子由「第一次減數分裂前期(prophase I)」進展到「第二次減數分裂間期(metaphase II)」(又稱為 oocyte maturation，在 ovulation 前就已經發生)
2. 卵子卵丘複合體(cumulus-oocyte complex, 簡稱COC)脫離濾泡壁(NSAID無法抑制)(此約發生於LH或hCG onset 後 34-36小時，所以是試管嬰兒療程之取卵時機)
3. Ovulation (足量的NSAID可抑制)
4. Ovulation後,濾泡壁上剩下的細胞(granulosa cell & theca cell)受到LH(或人工生殖中取代以hCG)作用而 luteinization 形成「黃體」-負責供應E & P,使子宮內膜得以完整地decidualization，開啟implantation window 俾利胚胎著床

Oocyte 卵子



LH surge

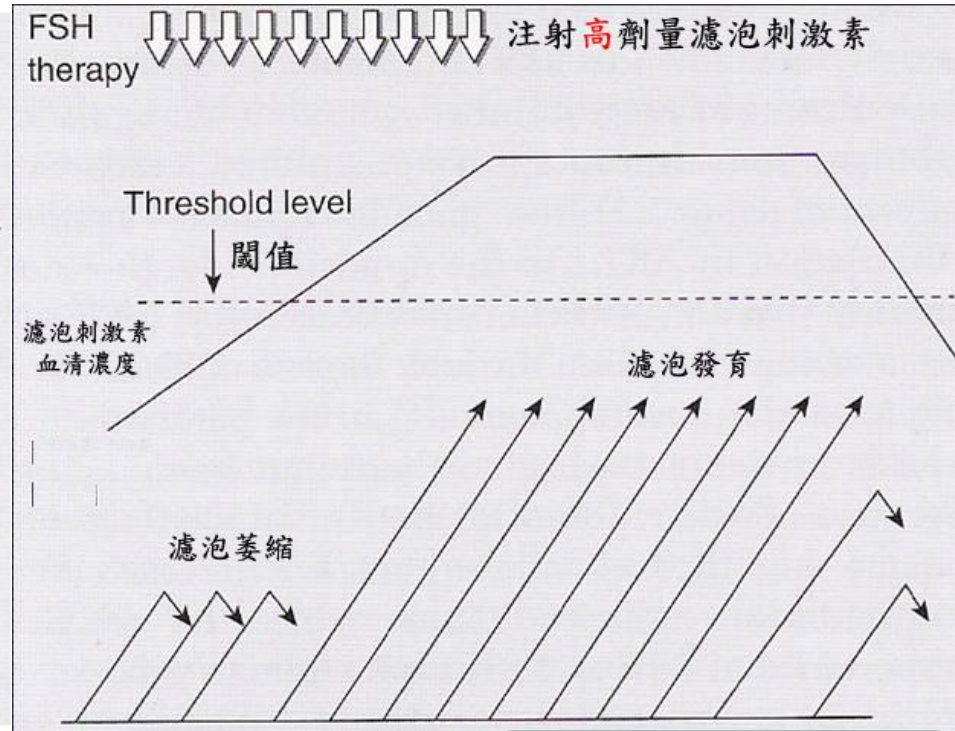
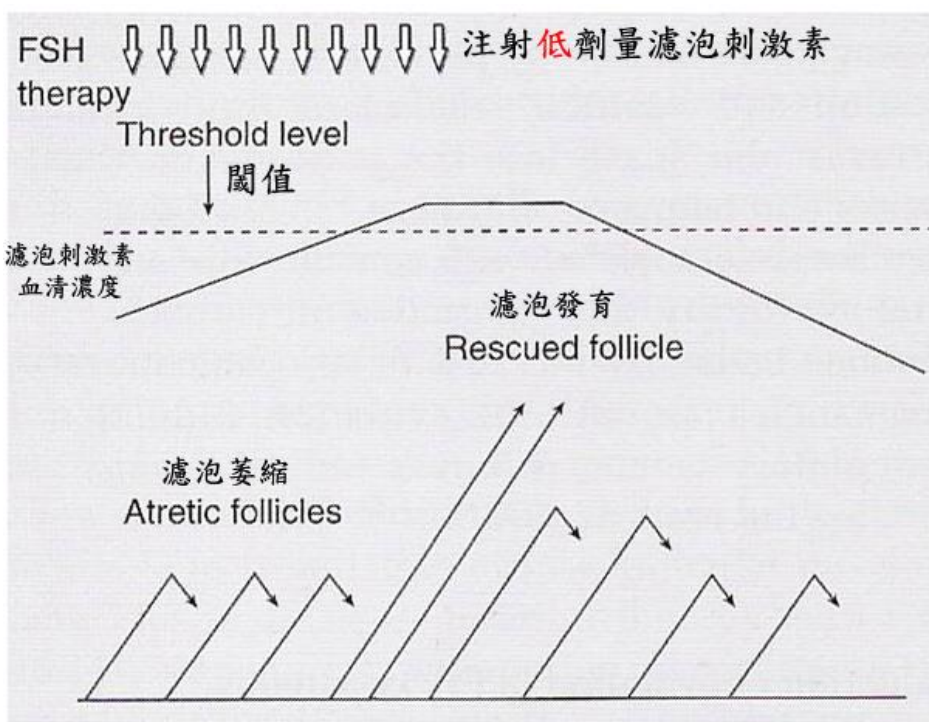
Meiotic Resumption (→ M II)



誘導排卵 (Controlled ovarian stimulation)

人工授精：**1~3個**濾泡發育

試管嬰兒：**8~15個**濾泡發育



follicles development(養濾泡) trigger final oocyte maturation (破卵)
for 7-9 days or more →

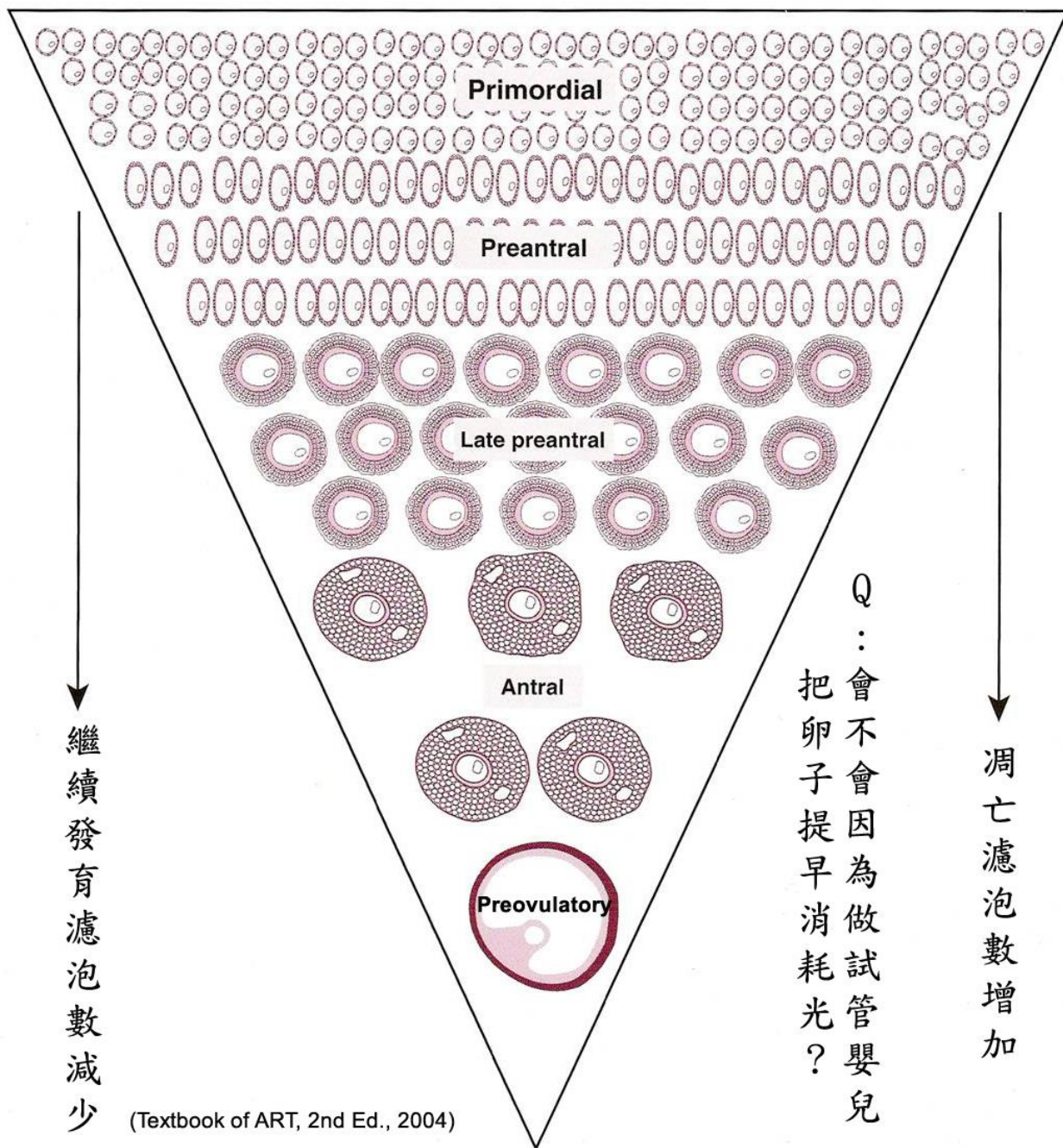
(controlled ovarian stimulation by rFSH)

34- 36 hours

人工授精
或自行同房

黃體期補充

一次誘發多個濾泡，
會加速卵量衰竭？
而提早停經嗎？



(Textbook of ART, 2nd Ed., 2004)

Drugs for ART

- 口服: Clomiphene citrate or Letrozole
- 皮下注射: Follicle-stimulating hormone (FSH)
Puregon(保妊康)/Gonal-F(果那芬) / long-acting FSH (Elonva)
- 皮下注射: Human menopausal gonadotropins (HMG) Menopur(美諾孕) 、 rFSH+rLH Pergoveris(倍孕力)

「排卵藥」：
提升FSH+/-
LH(濾泡吃
這個長大的)

-
- Human chorionic gonadotropin (hCG) Ovidrel (克諾得)/Pregnyl(保健寧)
 - GnRH agonist Leuplin(柳菩林)/Decapeptyl(弟凱得)

取代/引發LH
（「破卵針」
& 卵子最後之
熟成）

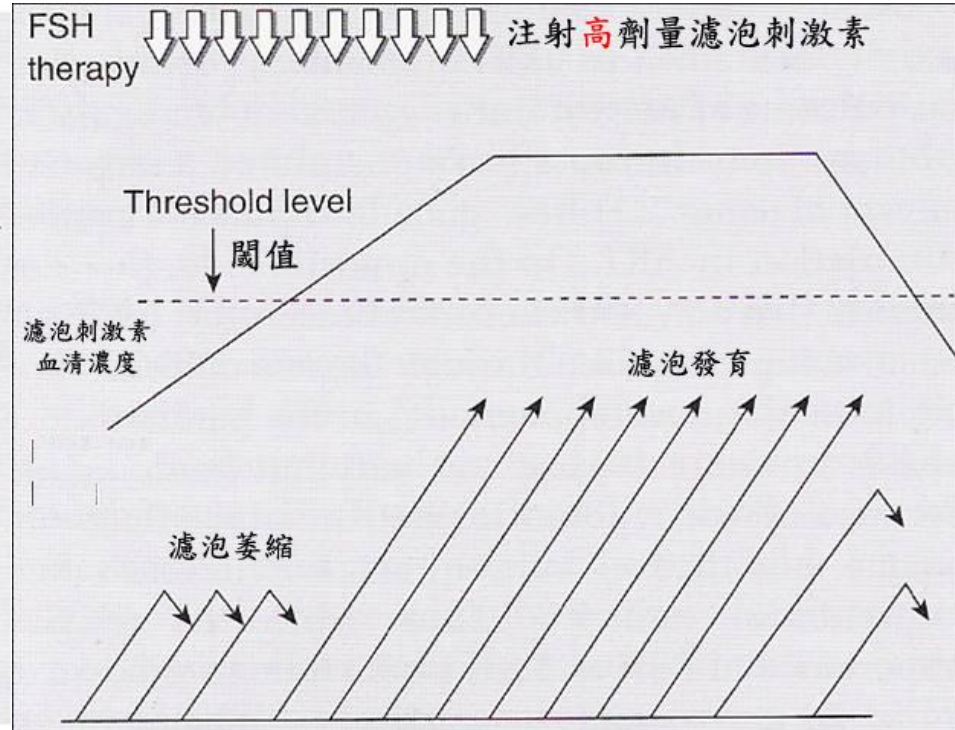
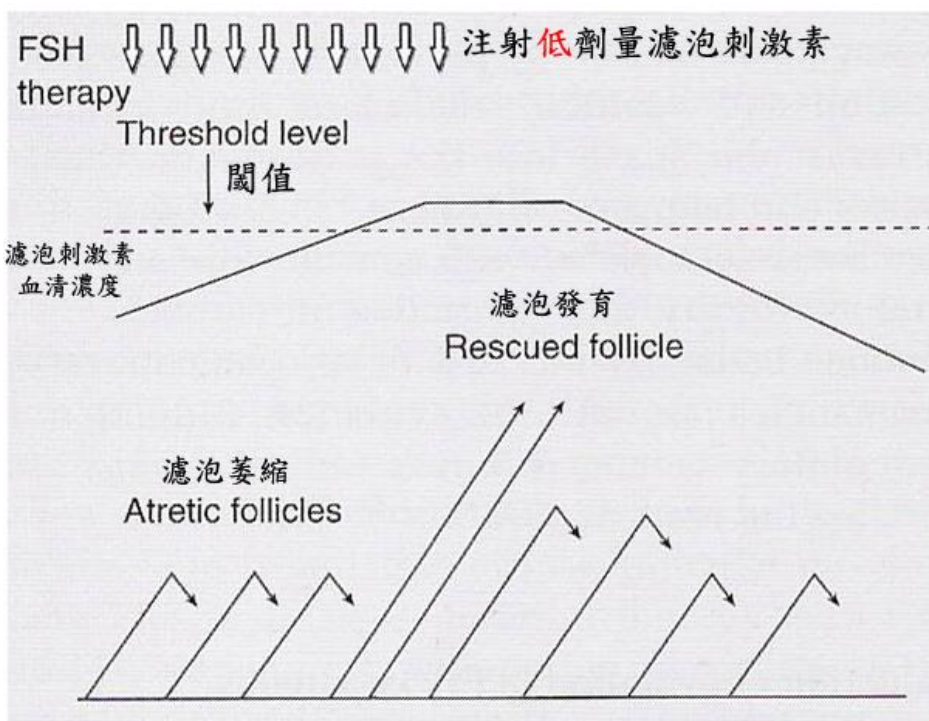
-
- Gonadotropin releasing hormone analogues (GnRH agonist) Leuplin(柳菩林)/Decapeptyl(弟凱得)
 - Gonadotropin releasing hormone analogues (GnRH antagonist) Orgalutron (柔妊孕)/Cetrotide (欣得泰)

擇一：預防LH提早上升

誘導排卵 (Controlled ovarian stimulation)

人工授精：**1~3個**濾泡發育

試管嬰兒：**8~15個**濾泡發育



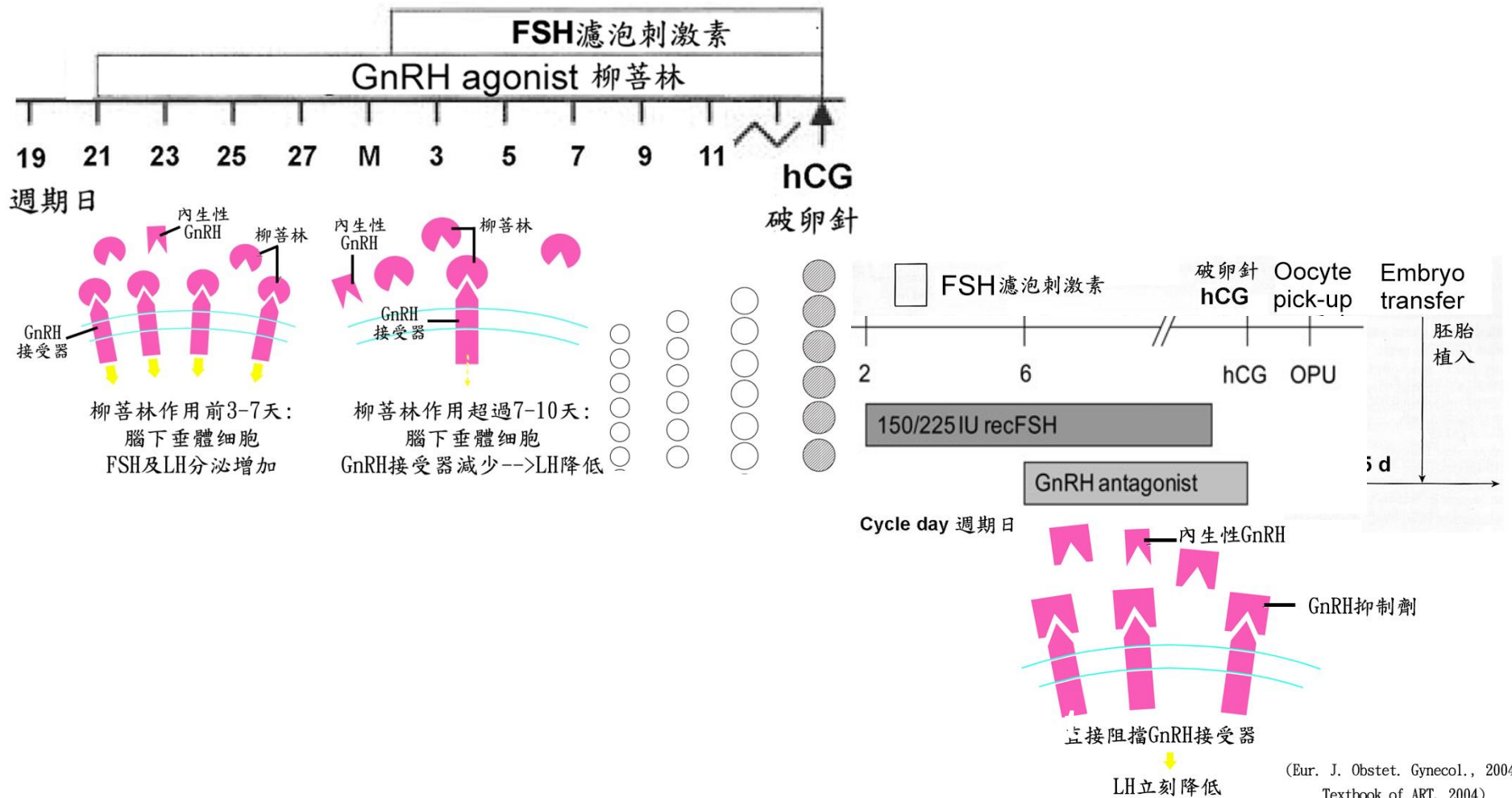
✳E2>200 pg/ml for > 50 hrs
會造成positive feedback，刺激LH大量分泌（LH surge）

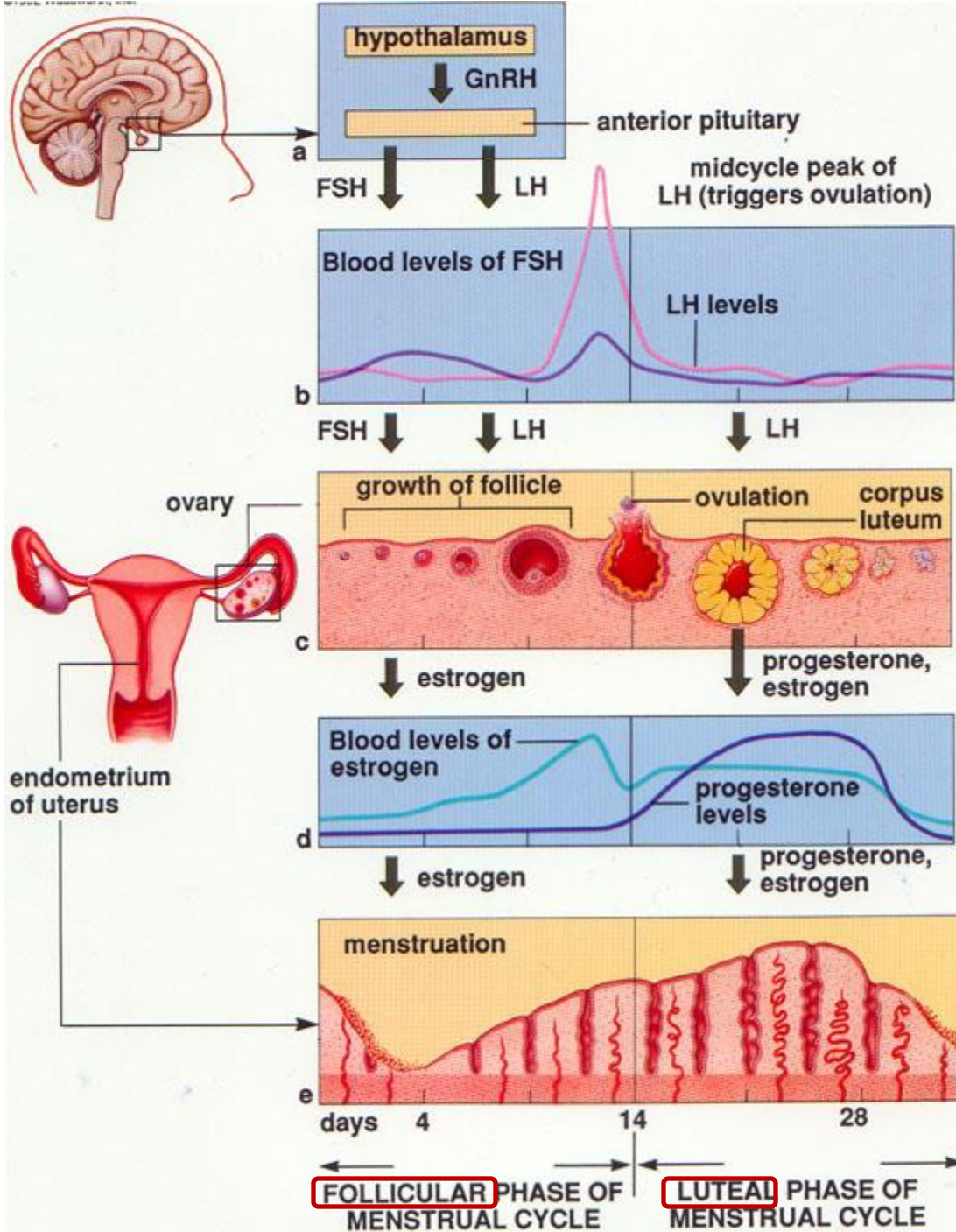
each follicle
沒有做好做滿
serum E2就可達帶動LH上升

GnRH agonist vs. GnRH antagonist:

「用法」異

「目的」同: **讓follicle做好做滿**

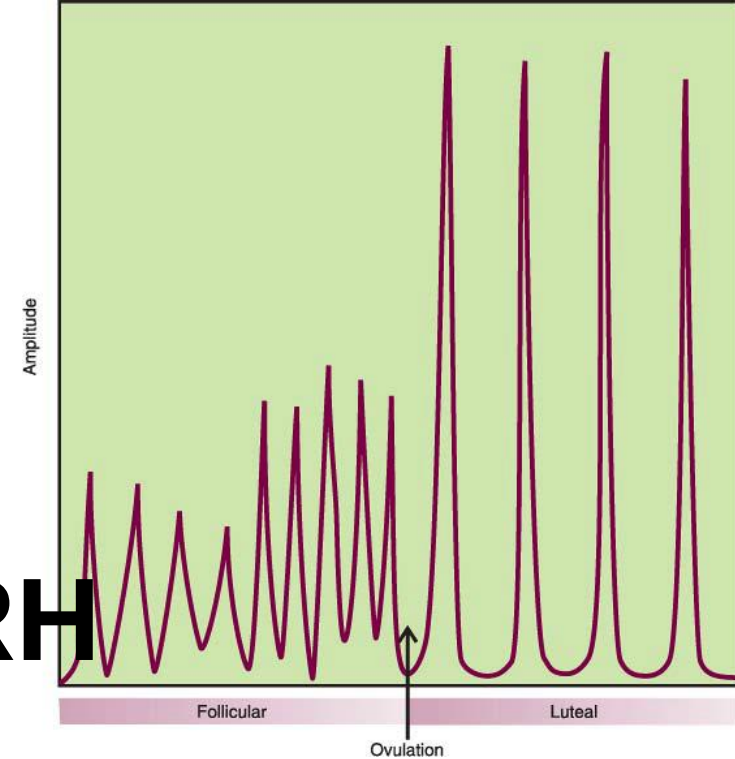




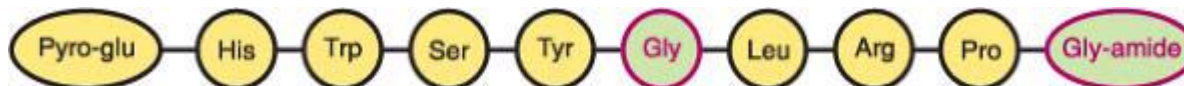
Pulsatile GnRH ($t_{1/2}$: 2-4 min)
(frequency)

→ FSH and LH in pituitary gland
→ Ovary: follicular growth, ovulation
and corpus luteum formation
→ Estrogen and Progesterone
affects the endometrium

Hypothalamus: GnRH



- **GnRH (Gonadotropin Releasing Hormone)**
 - 半衰期短: 2~4 min
 - produced in the arcuate nucleus of the hypothalamus, in a **pulsatile fashion**
 - Control FSH/LH by different frequency
 - 排卵前: 強度短小而密
 - 排卵後: 強度高而間隔長(3~4 h)
 - Decapeptide



GnRH and GnRH-R binding

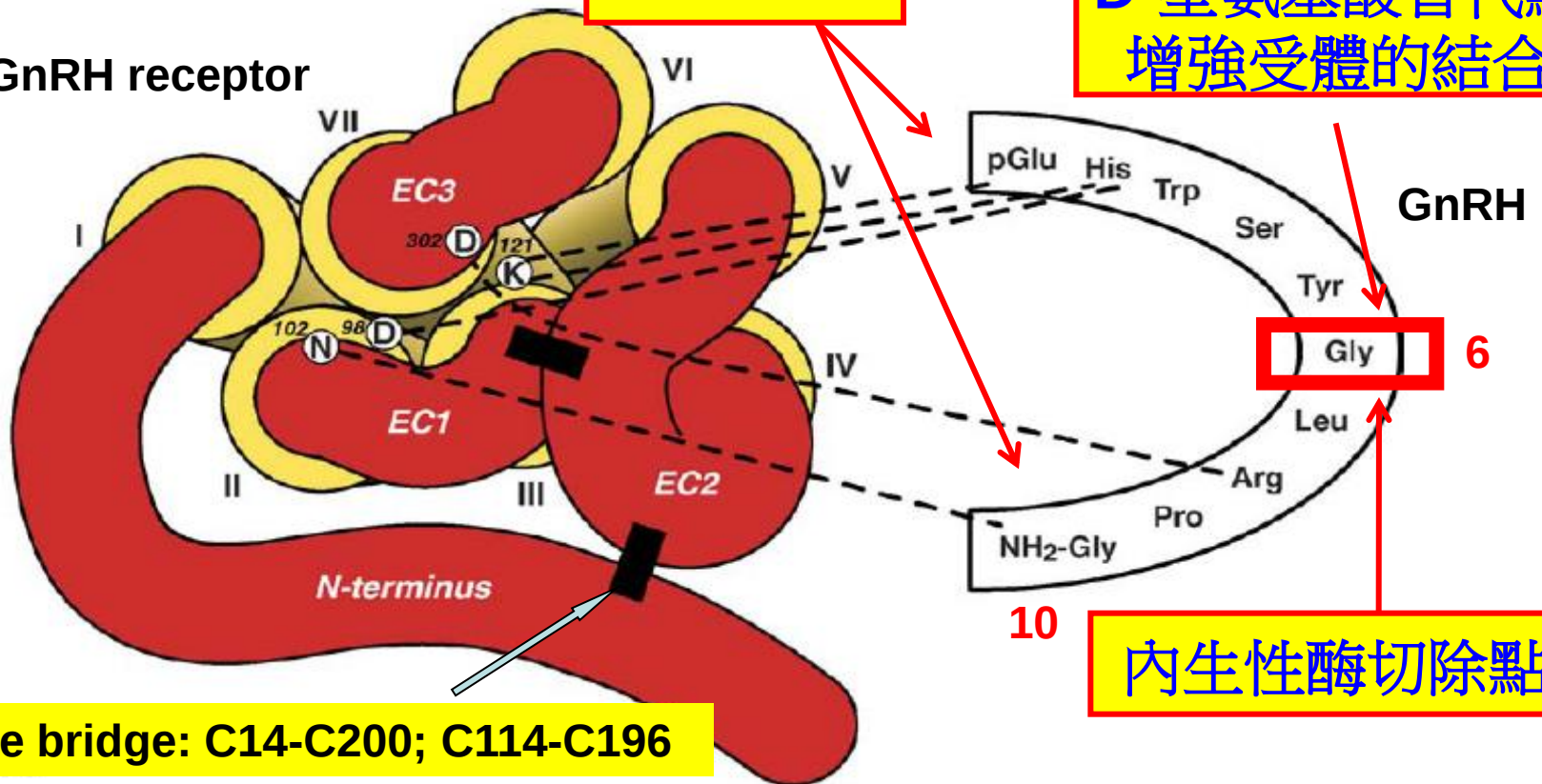
328 amino acids

Deca-peptide

受體結合區

D-型氨基酸替代點
增強受體的結合

GnRH receptor



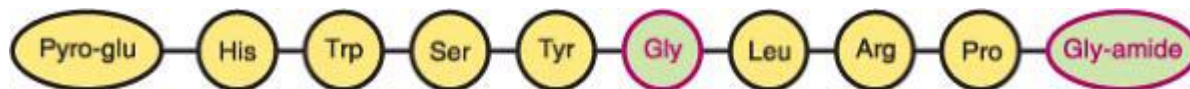
Disulphide bridge: C14-C200; C114-C196

Modifications

- **Position 6:** ↓ enzymatic degradation
- **Position 10:** ↑ potency
- **Position 6 and 10:** ↑ receptor affinity

王鵬惠

GnRH 類似物



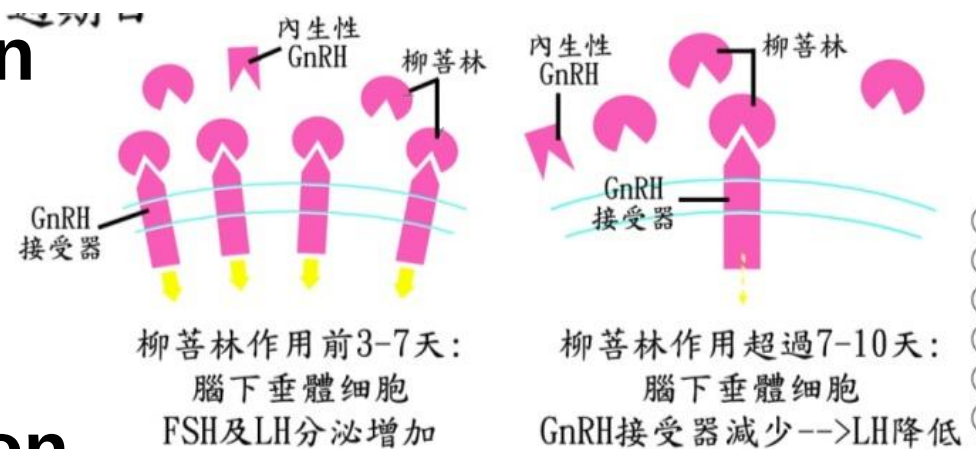
— 臨床藥物 GnRH agonist

-- ex. AA 6 modification

→ Long acting,
desensitize

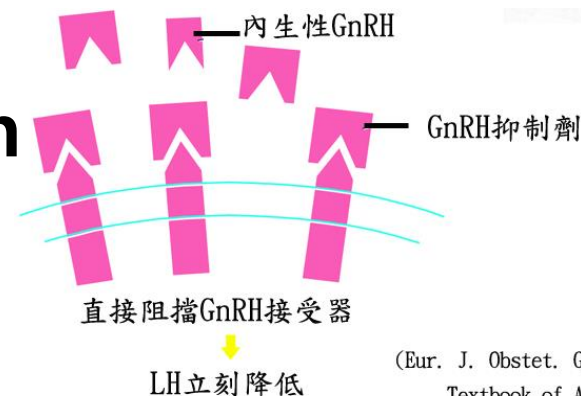
GnRH receptors

after days of stimulation



• 臨床藥物 GnRH antagonist

- - AA 1,2,3,6,8,10 modification



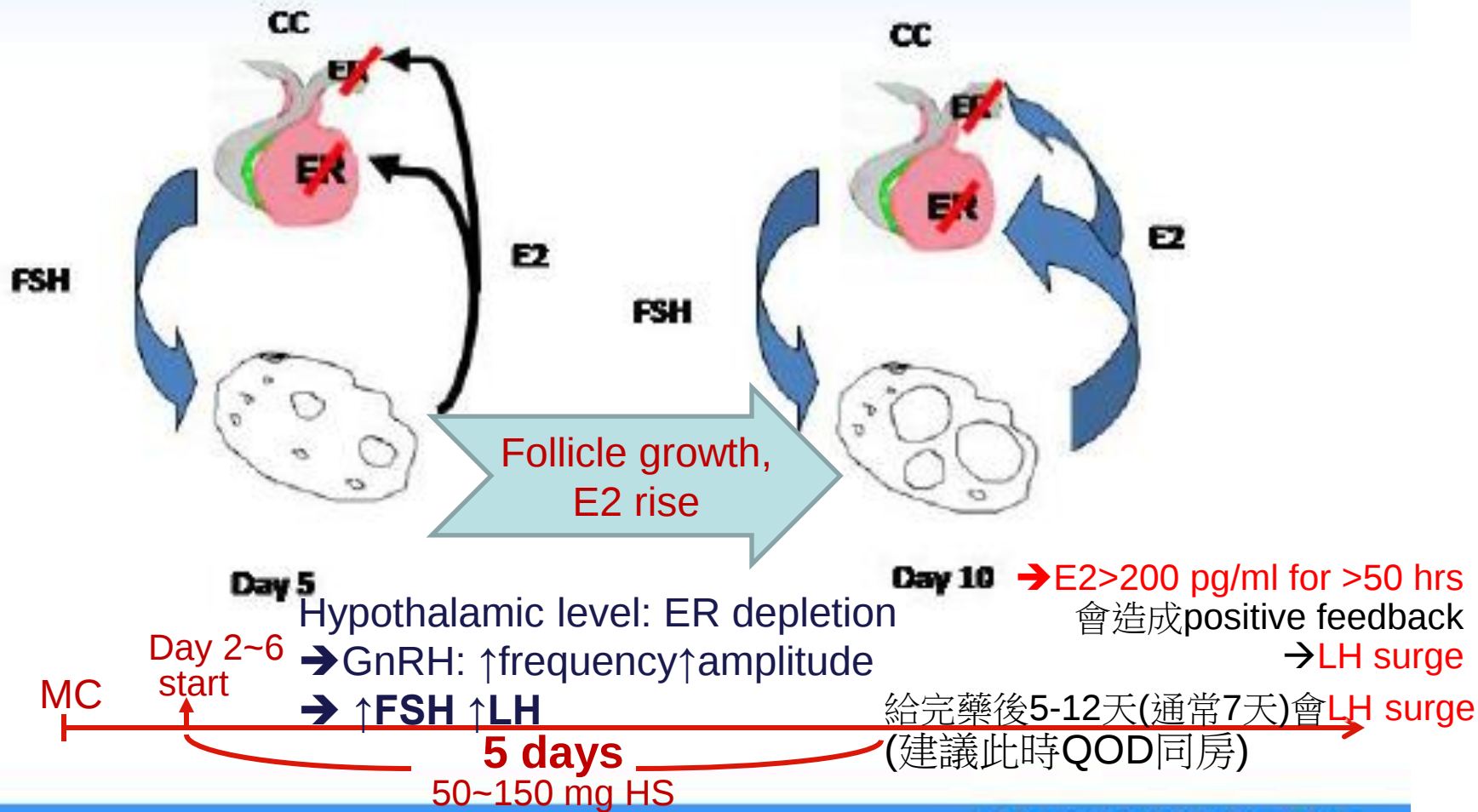
- Ovulation induction/ Controlled ovarian hyperstimulation
 1. Oral
 2. Injection sc

「排卵藥」:提升FSH+/-LH



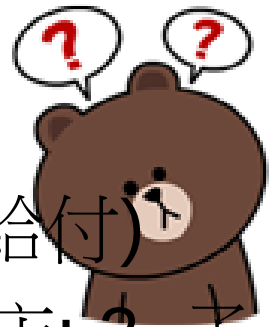


Clomiphene Citrate Treatment



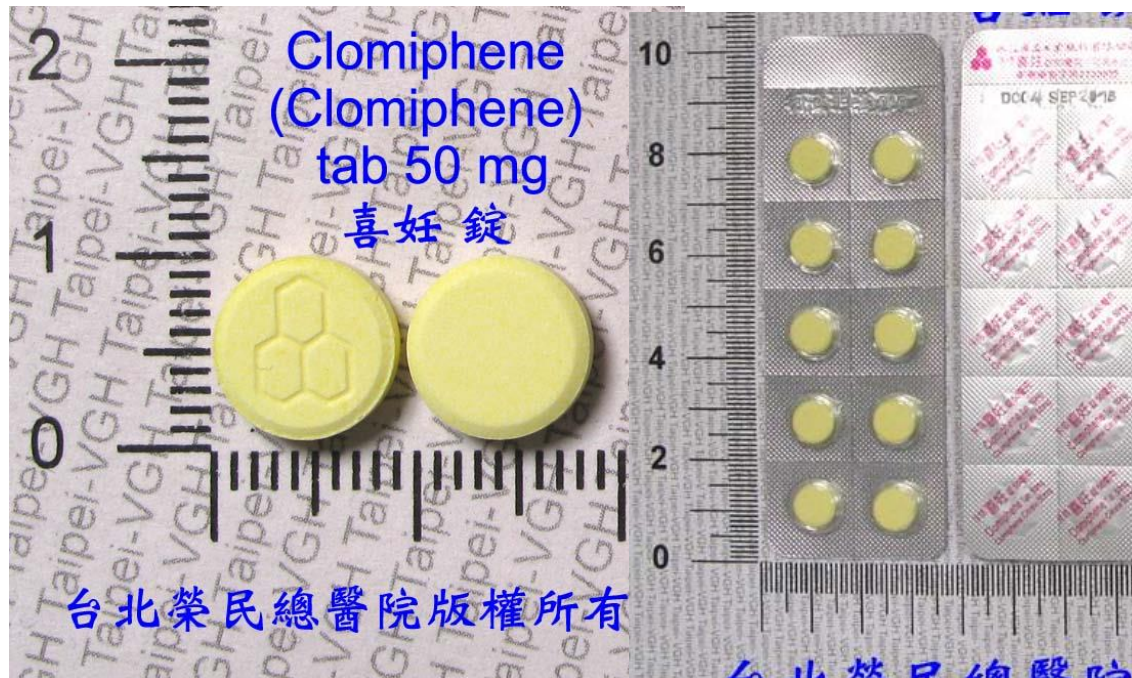
Casper and Mitwally

慢性不排卵（月經不準時，愛愛日好難算！）



第一線口服排卵藥：喜妊(Clomiphene) (健保給付)

--可能面臨問題：1. 子宮內膜太薄而不利於著床；2. 子宮頸黏液較不利於精子進入(自然同房者)；3. 至多六週期；4. BMI高；5. 胰島素阻抗高 效果差



102年第二次專技醫師二醫學六

關於口服排卵藥物clomiphene citrate，下列敘述何者最正確？

- A. 需使用於hypothalamus-pituitary axis功能失調的女性
- B. 具強效的雌激素作用
- C. 會減少GnRH分泌
- D. 會使子宮內膜變薄

D

103年第一次專技高考

醫師(一)醫學(二)

下列有關 **clomiphene** 的藥理學作用描述，何者錯誤？

- A. 為一種雌激素受體部分作用劑（**partial estrogen agonist**），可以刺激促性腺激素（**gonadotropins**）的分泌作用
- B. 對於排卵功能障礙的婦女具有刺激排卵的作用
- C. 使用時會降低血漿中黃體化激素（**LH**）和濾泡促進素（**FSH**）的濃度
- D. 容易誘發熱潮紅（**hot flushes**）的產生

C

第二線口服排卵藥物：復乳納Letrozole (自費)

- 沒有Clomiphene的副作用，而且成功率和Clomiphene並駕齊驅。
- 罹患乳癌卻仍想生育的婦女
- 可能有些潛在的副作用尚未被發現。但以目前的研究證據看來，Letrozole並沒有造成比Clomiphene多的胚胎異常。

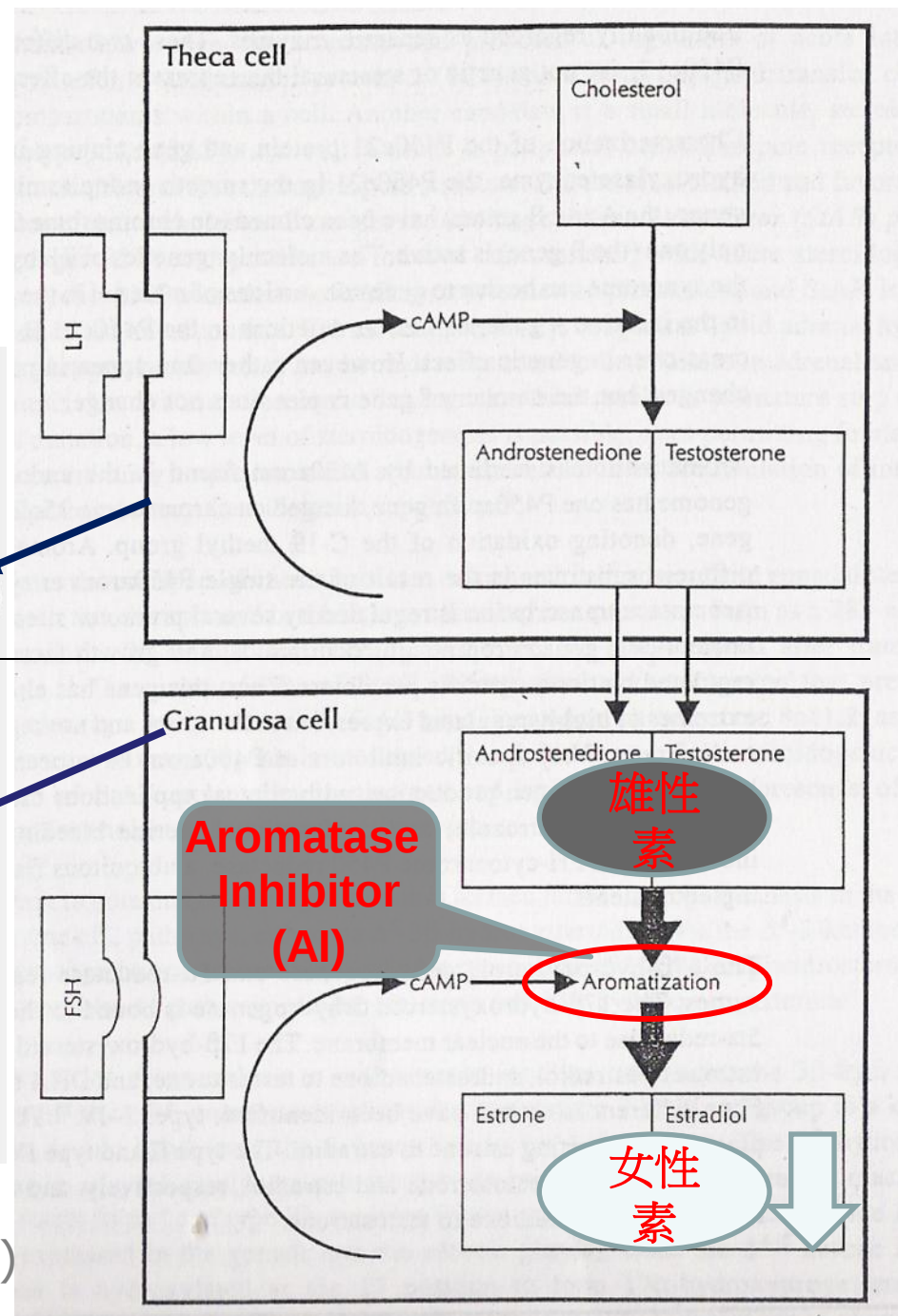
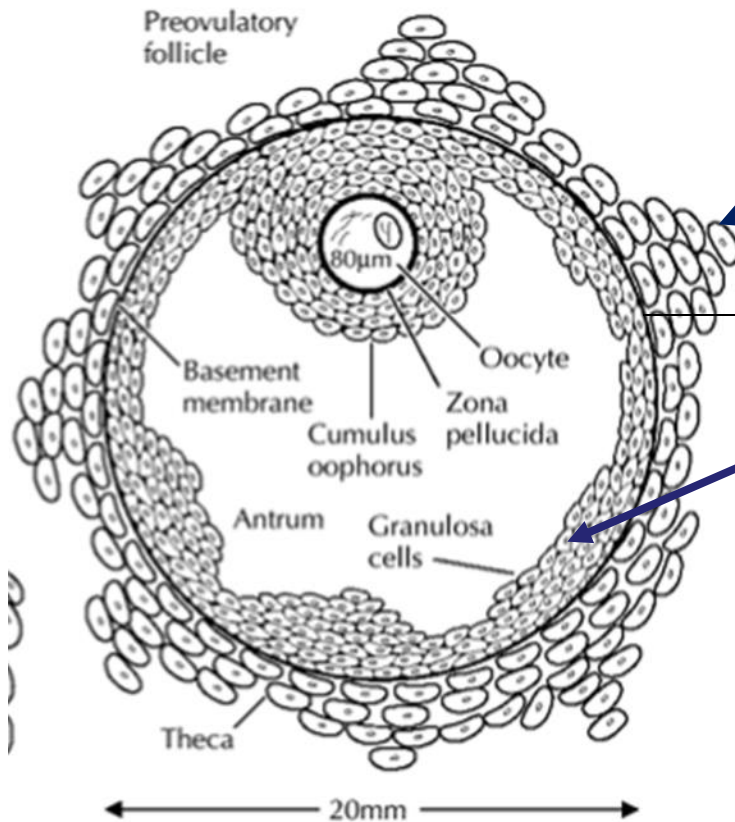


台北榮民總醫院版權所有



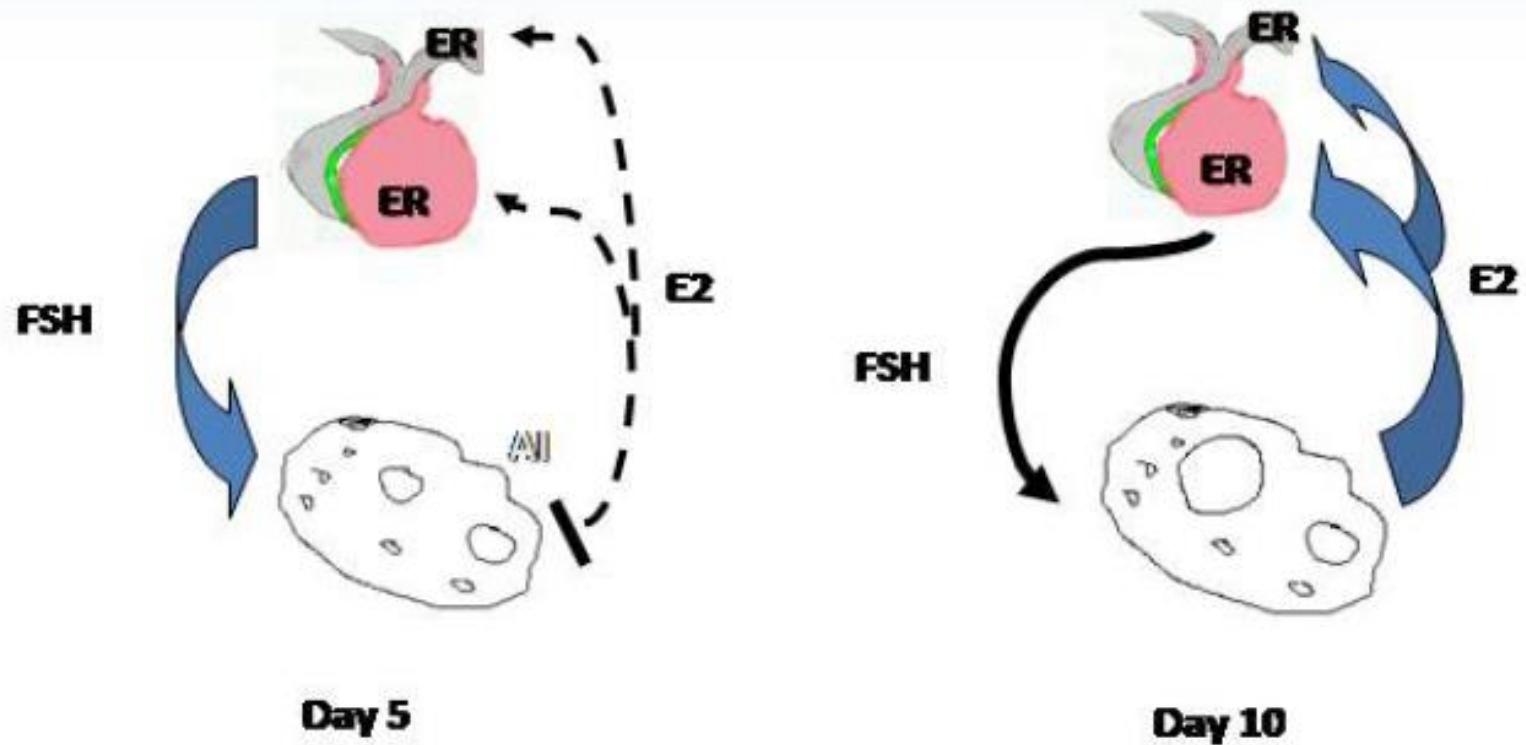
台北榮民總醫院版權所

Two Cell- Two Gonadotropin Theory



(Clin. Gynecol. Endocrinol. Infertil., 6th Ed.)
(Textbook of ART, 2nd Ed., 2004)

Aromatase Inhibitor Treatment



輸卵管有通, 可先嘗試自然同房 ／人工受精

- 亦要考慮年齡因素(卵子品質的關鍵所在)

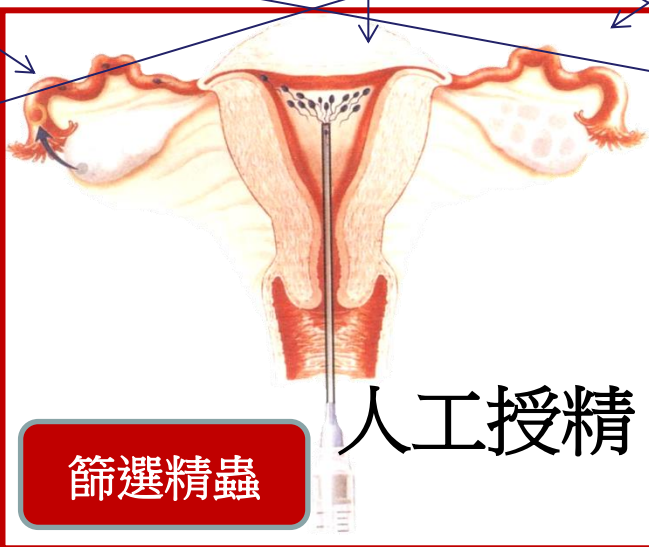
幫助排卵的藥物



排卵針

自然同房

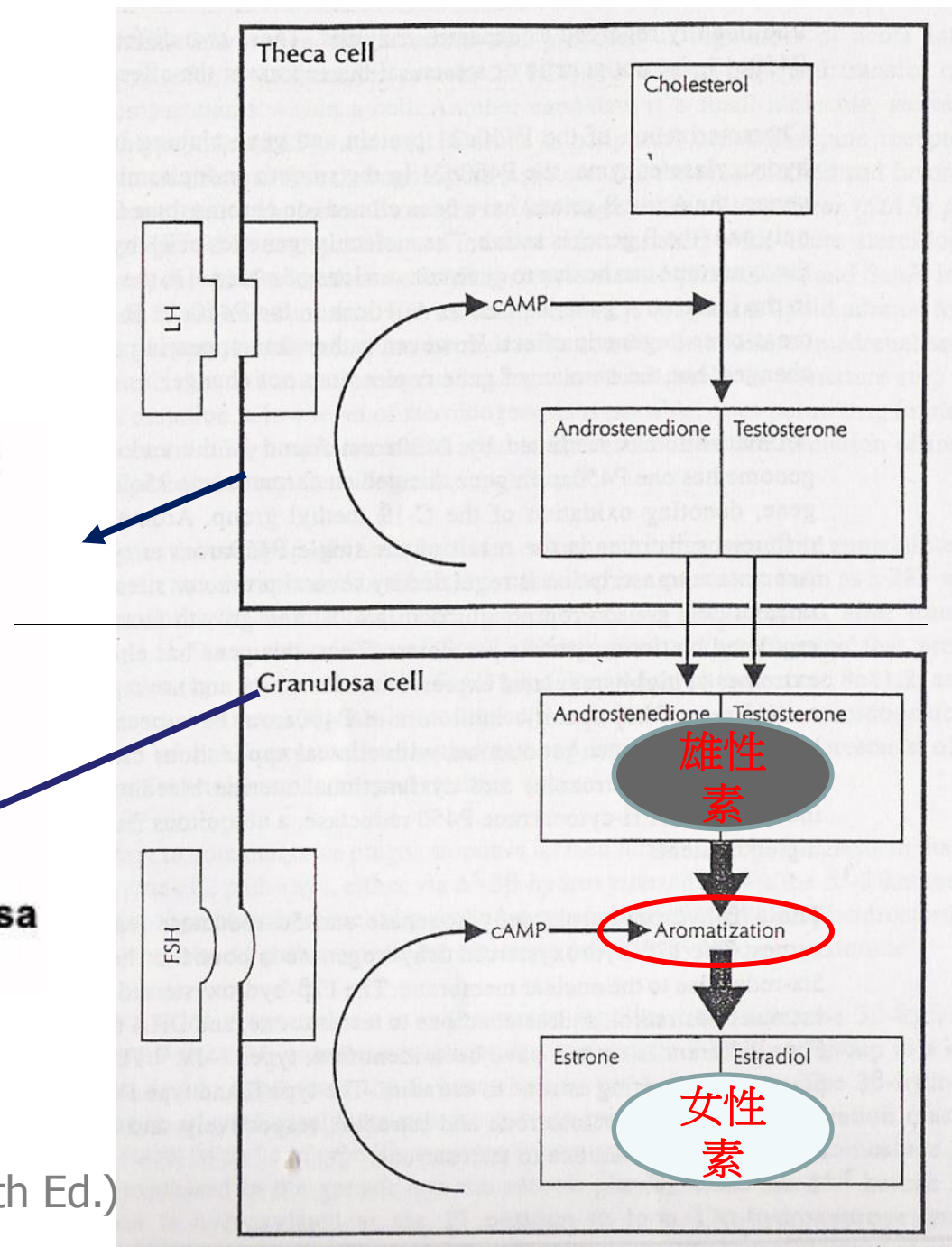
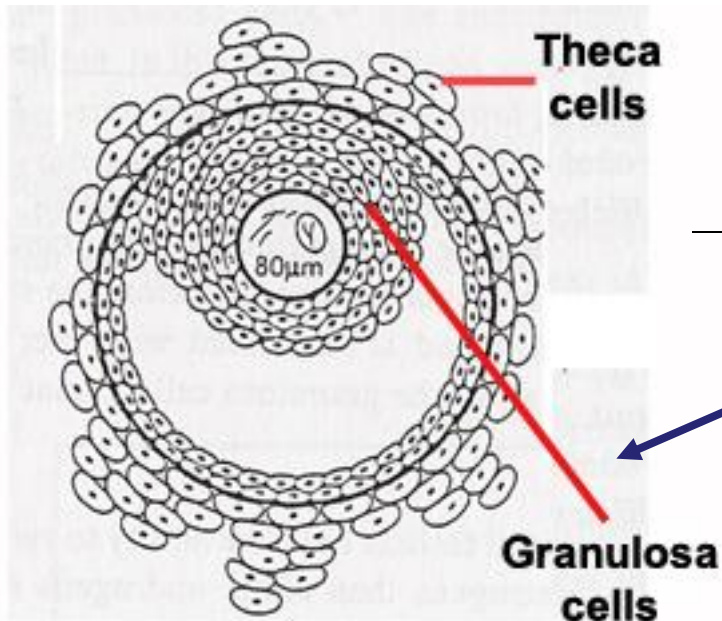
精卵相遇的途徑



試管嬰兒
(\$\$ >, <)

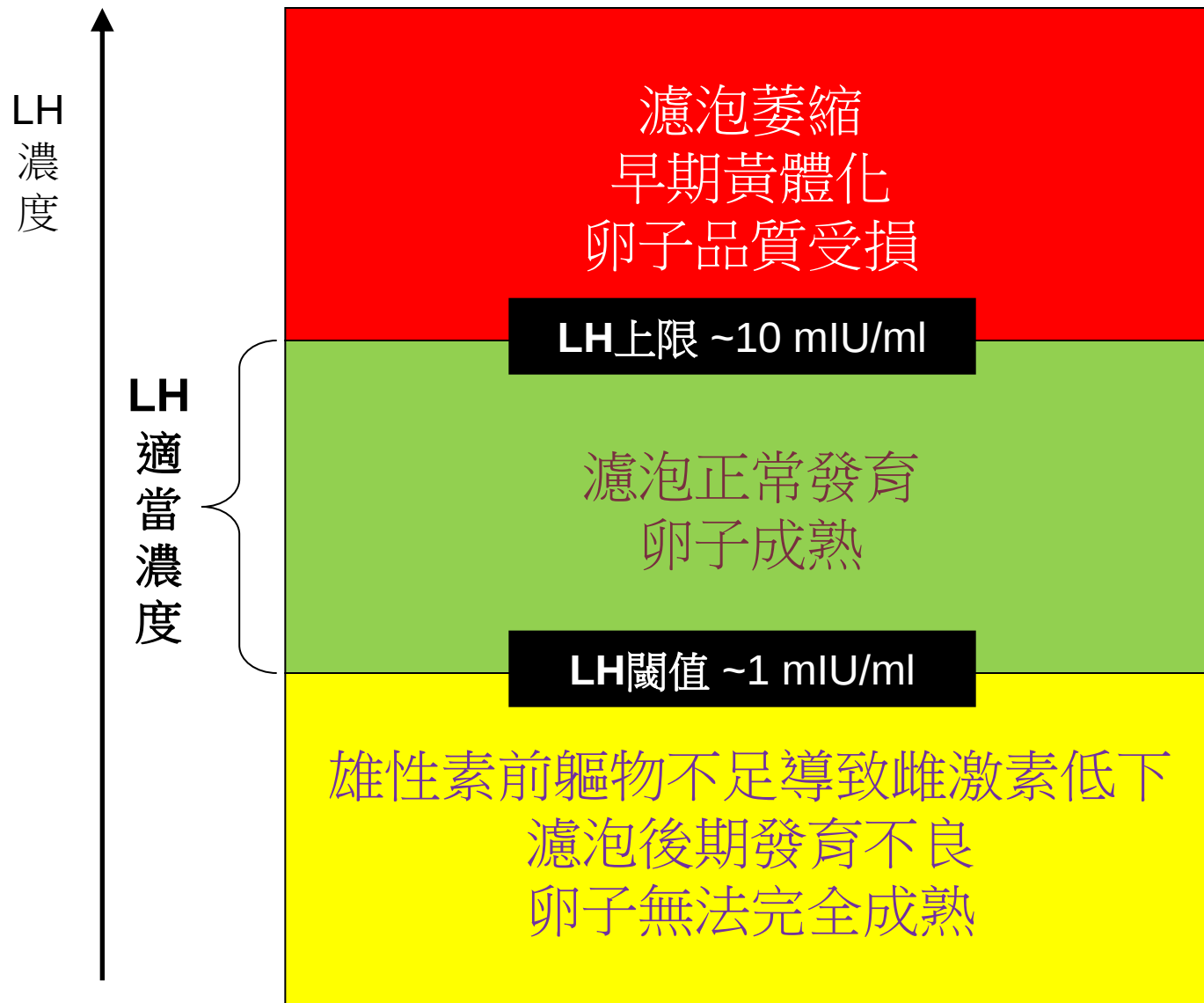
輸卵管不通/嚴重精蟲問題/前述方式失敗

Two Cell- Two Gonadotropin Theory



(Clin. Gynecol. Endocrinol. Infertil., 6th Ed.)
(Textbook of ART, 2nd Ed., 2004)

黃體刺激素（LH）在誘導排卵的角色



在不使用GnRH-a
或GnRH-ant時，
**FSH誘導排卵約有
20%會發生LH早期
上升**

下視丘/腦下垂體疾病
或使用GnRH-a depot
，可能導致LH不足

High LH Levels are Unfavorable to Reproductive Outcome

- High endogenous LH: increased incidence of infertility and miscarriages
- LH inhibits granulosa cell proliferation at high concentrations, and induce atresia of follicles
- LH has a negative effect on the endometrium

各種protocol之介紹

Ovulation induction

提升**FSH +/- LH**養卵泡



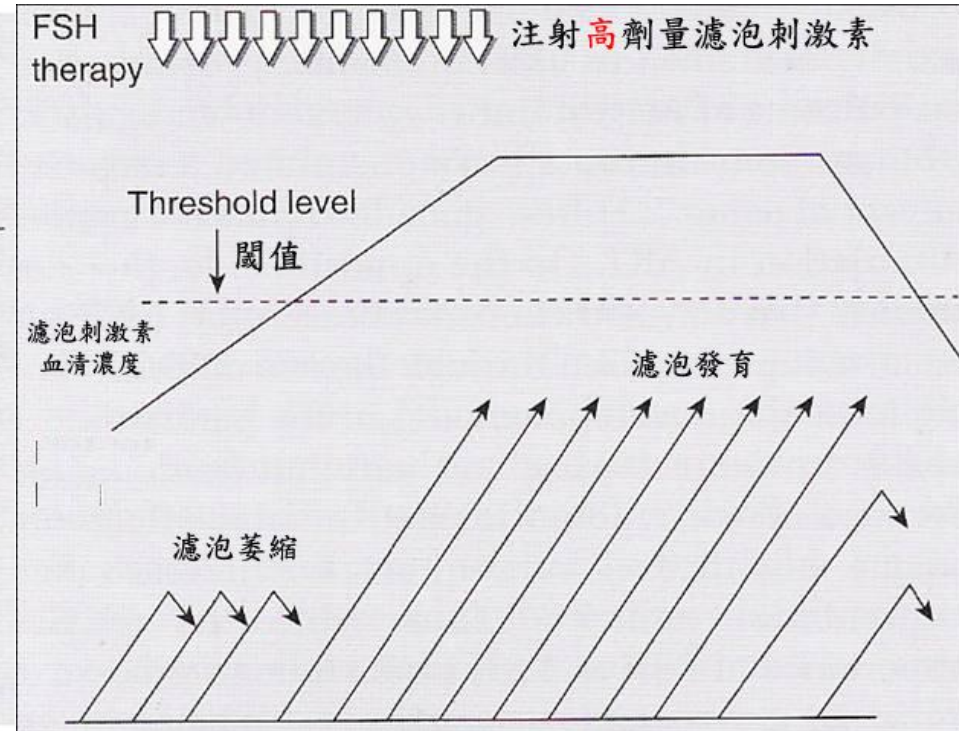
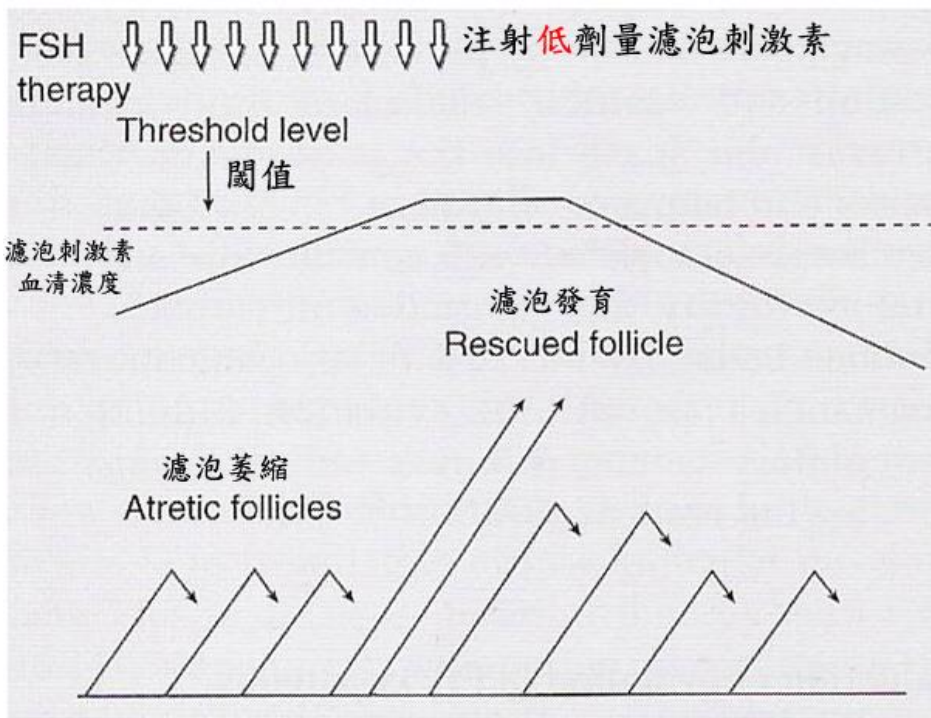
To prevent LH premature surge

預防LH提早上升
(**PREMATURE LUTEINIZATION**)

誘導排卵 (Controlled ovarian stimulation)

人工授精：**1–3**個濾泡發育

試管嬰兒：**8–15**個濾泡發育



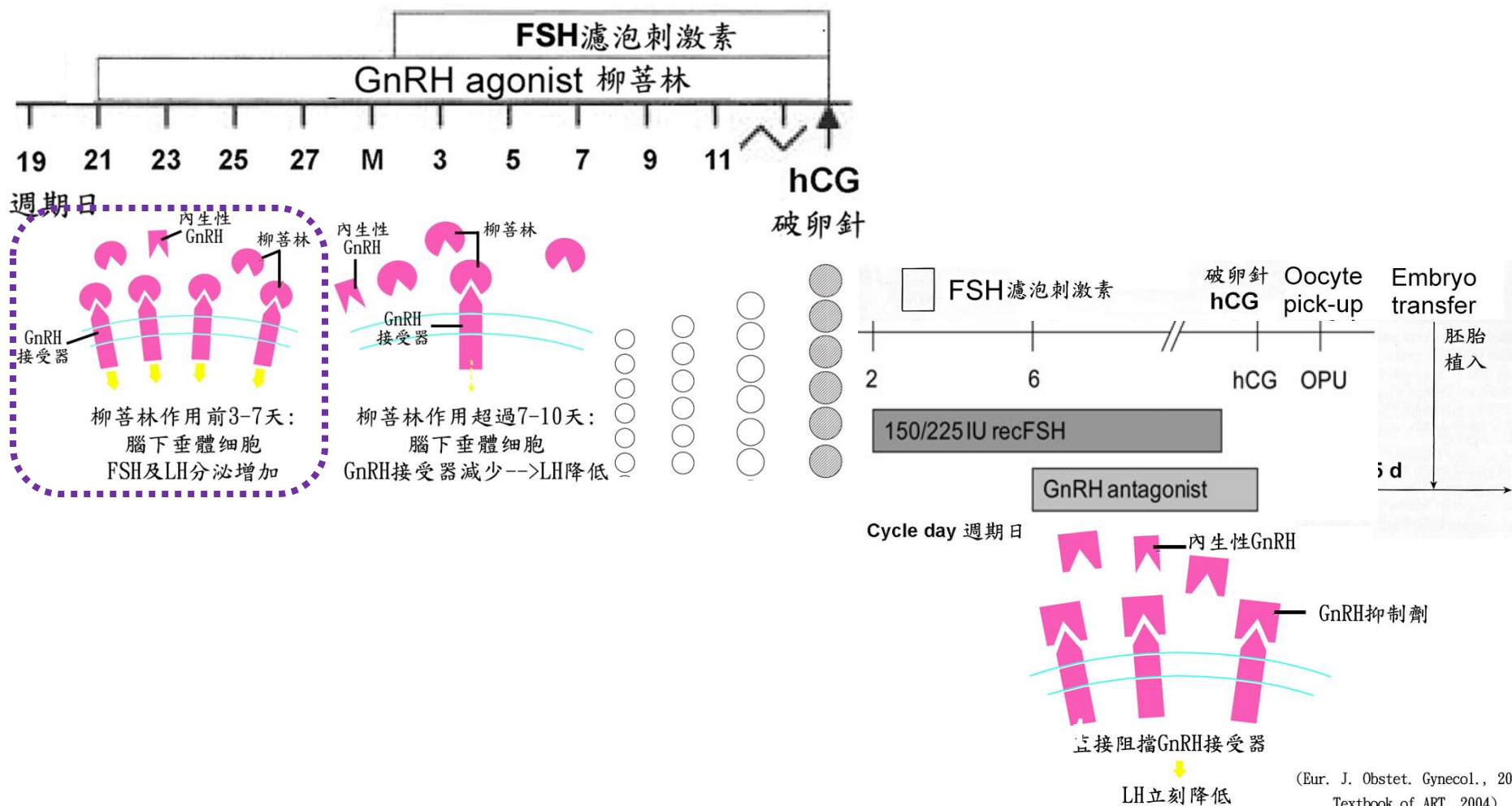
✳E2>200 pg/ml for > 50 hrs
會造成positive feedback，刺激LH大量分泌（LH surge）

濾泡還不夠熟
就發生了!!

GnRH agonist vs. GnRH antagonist:

「目的」同:預防LH提早上升

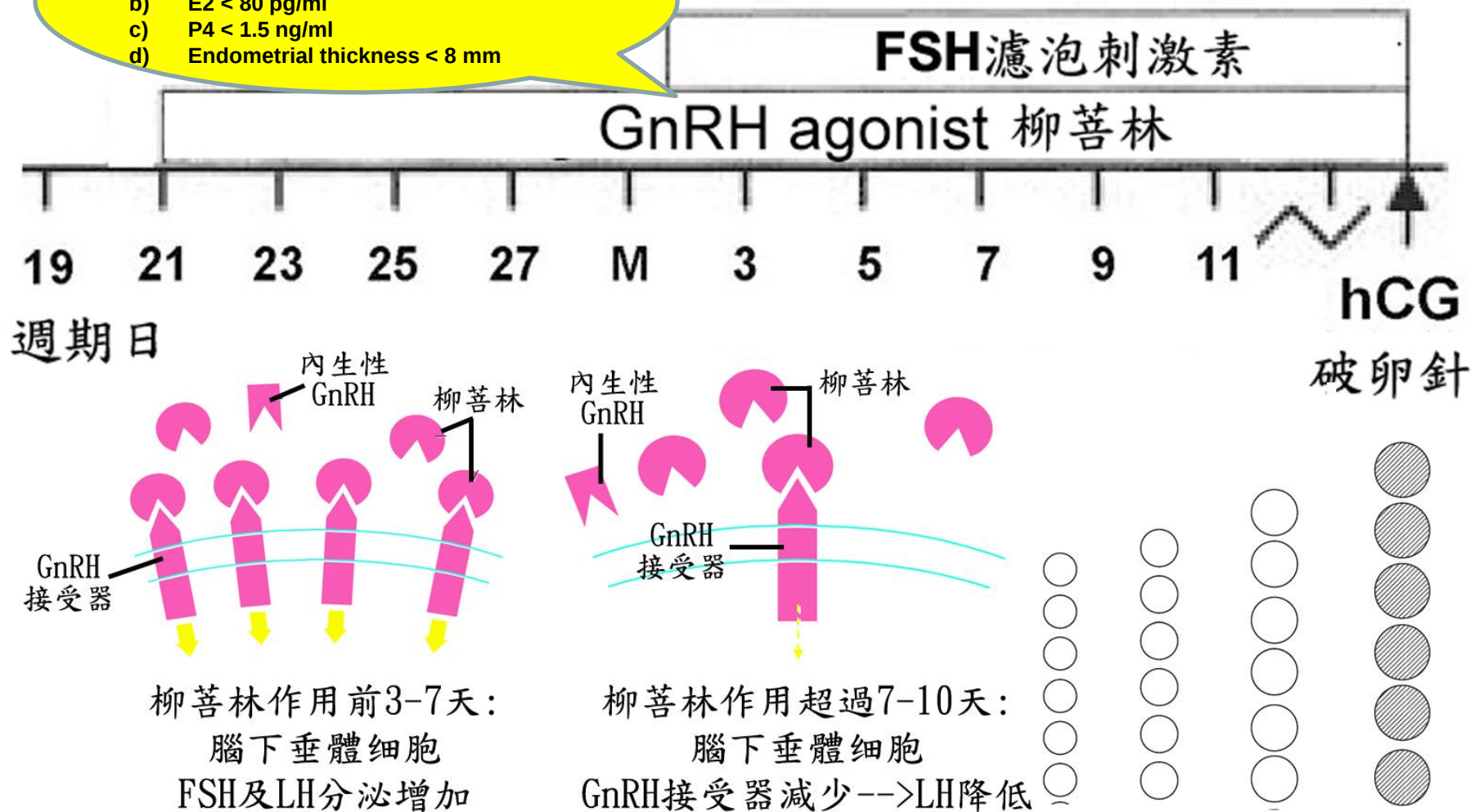
「用法」異



長療程 (Long protocol)

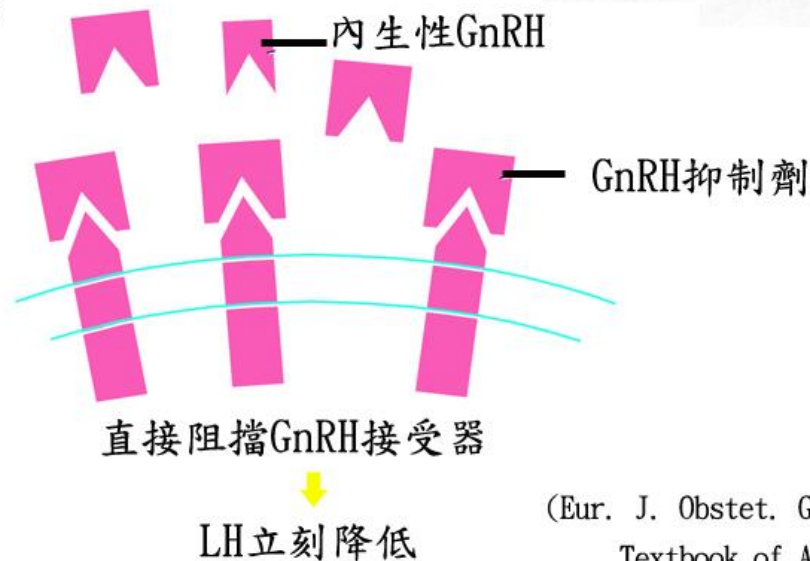
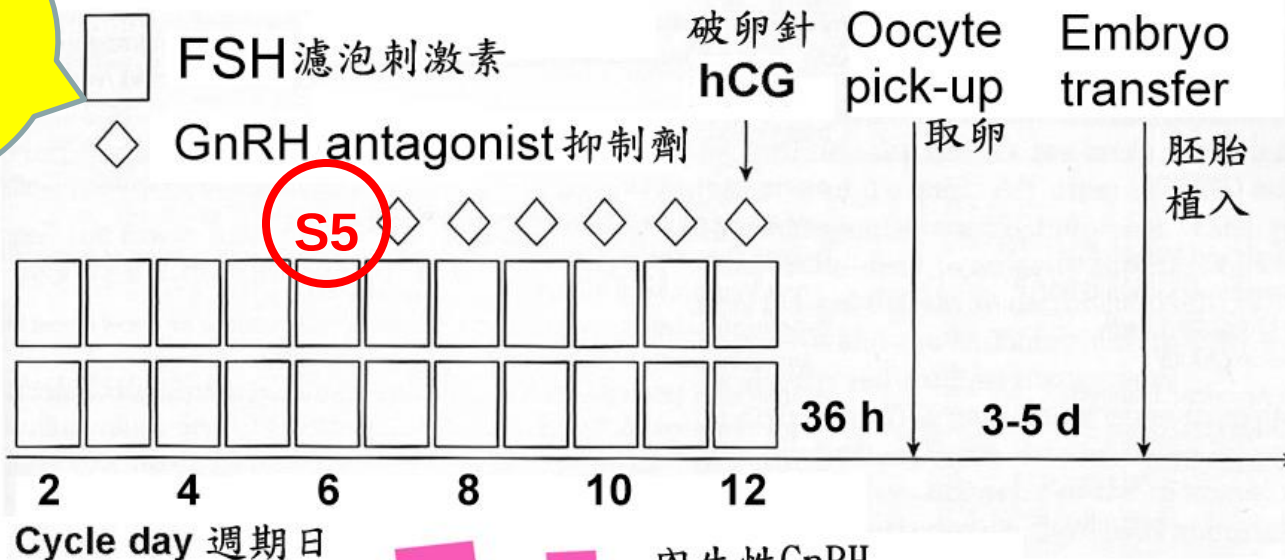
Monitoring of Pituitary down-regulation:

- a) Menstrual bleeding
- b) $E2 < 80 \text{ pg/ml}$
- c) $P4 < 1.5 \text{ ng/ml}$
- d) Endometrial thickness $< 8 \text{ mm}$



抑制劑療程 (Antagonist protocol)

Better start from MC day 2-3 (early follicular phase $\leq$ 5th day, no dominant follicular yet. The earlier, the more follicles)



(Eur. J. Obstet. Gynecol., 2004;
Textbook of ART, 2004)

93年第一次專技高考 基礎二

有關gonadotropin-releasing hormone (GnRH) 之敘述中，下列何者正確？

- A. 其由腦下垂體產生
- B. 為一種多胜 (poly-peptide) 組成
- C. 長期大量給與GnRH 類似物，會產生生殖腺官能不足
- D. 持續大量給與GnRH 類似物，會使GnRH 接受器之敏感性加強

BC

C關於目前用於刺激排卵的GnRH-agonist，
下列敘述何者正確？

A長療程（long protocol）乃利用其up-regulation特性

B和內生性GnRH比較，只有1個氨基酸不同

C半衰期比內生性GnRH長

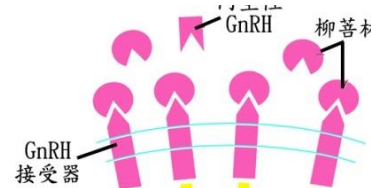
D可口服使用

誘導排卵

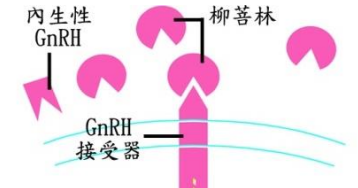
Long luteal

Cycle day 15 17 19 21 23 25

with GnRH agonist



柳菩林作用前3-7天:
腦下垂體細胞
FSH及LH分泌增加

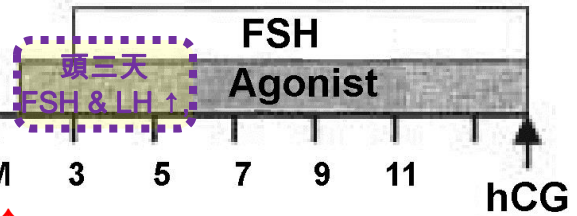


柳菩林作用超過7-10天:
腦下垂體細胞
GnRH接受器減少-->LH降低

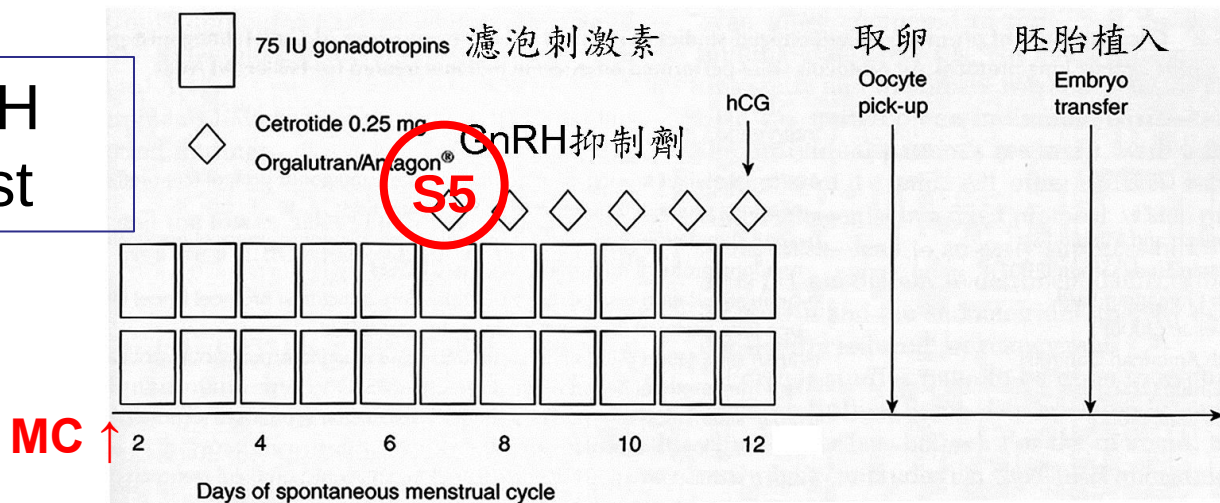
Short / flare-up

Cycle day 15 17 19 21 23 25 27 M 3 5 7 9 11

MC ↑



with GnRH antagonist



(Textbook of ART, 2nd Ed., 2004; Semin. Reprod. Med., 2002)

SOAP

(1)台北榮總婦產部 第一聯單位簽收聯 04類 其他

婦產科上午 082-01 1010329 健保卡序號:IC1010009 一般門診 收費序號:0839 13

2422193-0陳瓊瑤

一般健保

年齡:043歲女 電話:



身分證號:C220812***

S:43 Y/O, GPO, LMP: 101-3-28, 100-12-25, 100-10-13, 100-9-14, 100-8-13,
100-7-15,

100-6-19, D/I:

3/26

WANT A BABY

O:ICSI WITH FSH/HMG + GNRH-ANTA

IVF WITH GNRH-A + FSH/HMG: POOR FERTILIZATION BY IVF, ICSI REQUIRED

D3 BLOOD TESTS: WNL

D3 TVS: AFC 8

CBC/PT/APTT: WNL

VDRL AND HIV: NEG. FOR THE PATIENT

HSG: X-ray evidence of patency of bilateral fallopian tubes is

李新揚 3643H

seen. Bilateral fallopian tubes are normal in this examination.
X-ray evidence of small linear filling defect in the right
upper lateral portion of the uterus is seen.

SA: 15.2 M, 39%, 53%, MAR -/-

HYSTROSCOPY + D&C: WNL, NPD

PLEASE CHECK ANTRAL FOLLICLE COUNTS

Please check antral follicle counts

A:628.9 INFERTILITY, FEMALE

252.8 OTHER DISORDERS OF THE PITUITARY/HYPERPROLACTINEMIA



施行人工生殖用藥療程暨濾泡檢驗單

7F

姓名	陳瑞雄	病歷號	2420193 -	連絡電話	(44) 0921-611131 (H) 2637-2567
年齡	43	診斷	ICSI Male factor + poor ovarian reserve	主治醫師	主治醫師 李新揚 3643H

Mens & OBS Hx: LMP 101.03.28, PMP, G 0 P 0

Purpose: ☐ Ovulation induction/monitoring only ☐ AIH ☒ IVF/ICSI ☐ Other

Treatments

月經週期	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
月/日	3/8	3/9	3/10	3/11	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8				
核醫抽血檢驗						✓			✓							
濾泡超音波檢查						✓			✓							
Mercilon (美適儂)	口服															
Leuplin (柳菩林)	皮下; 午															
Cetrotide (欣得泰)	皮下; 上午							0.15	0.15	0.15						
Menopur (美諾孕)	皮下; 上午	1/2 + 2/3			150	150	150	150	150	150						
Gonal-F (果納芬)	皮下; 下午	6-9 PM			300	300	300	300	300	300						
Puregon (保妊康)	皮下; 午															
Pergoveris (倍孕力)	皮下; 午															

Lab. Finding:

Date	3/29	4/2	4/5	4/9	4/10	
Stimulation day						
E ₂ (pg/ml)	48.13	841	2994	取		
LH (mIU/ml)	5.16	3.72	3.37	取		
PGTR (ng/ml)	0.90	1.28	2.98	取		
Endometrial Thickness (mm)	6.8	4.1	9	①	ET	
Follicular Size	Rt	R0 23x22	16x9	22x12	8#	
		RF x7	15x8	15x10		
			10x9	15x9		
			7x8	10x7		
			6x6	7x6		
	Lt	L0 30x15	13x10	19x16		
		LF x7	9x7	19x12		
			8x8	17x10		
			8x7	17x9		
			8x5	16x13		
			6x4	10x9		
			4x4	9x7	9x7	

☒ Check health list☒ Check ID 王重煥 101.03.29

Controlled ovarian hyperstimulation: 用藥

行政院國軍退除役官兵輔導委員會臺北榮民總醫院

施行人工生殖用藥療程暨濾泡檢驗單

7F

姓 名	陳 琮 邊	病歷號	2422193 - ☐	連絡電話	(7) 0921-611131 (H) 2637-2567
年 齡	43	診 斷	ICSI Male factor + Poor ovarian reserve	主治醫師	主治醫師 李新揚 3648H

Mens & OBS Hx : LMP 101.03.28 , PMP _____ , G 0 P 0

Purpose : ☐ Ovulation induction/monitoring only ☐ AIH ☒ IVF/ICSI ☐ Other _____

Treatments

月經週期		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
月 / 日		3/8	3/9	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8				
核醫抽血檢驗							✓			✓							
濾泡超音波檢查							✓			✓							
Mercilon (美適儂)	口服																
Leuplin (柳菩林)	皮下; 午																
Orgalutron (柔妊孕)	皮下; 上午								0.25 mg	0.25	0.25						
Menopur (美諾孕)	皮下; 上午					150 IU	150	150	150	150	150						
Gonal-F (果納芬)	皮下; 下午					300 IU	300	300	300	300	300						
Puregon (保妊康)	皮下; 午																
Pergoveris (倍孕力)	皮下; 午																

Orgalutron (柔妊孕)

Controlled ovarian hyperstimulation: monitoring

Lab. Finding :

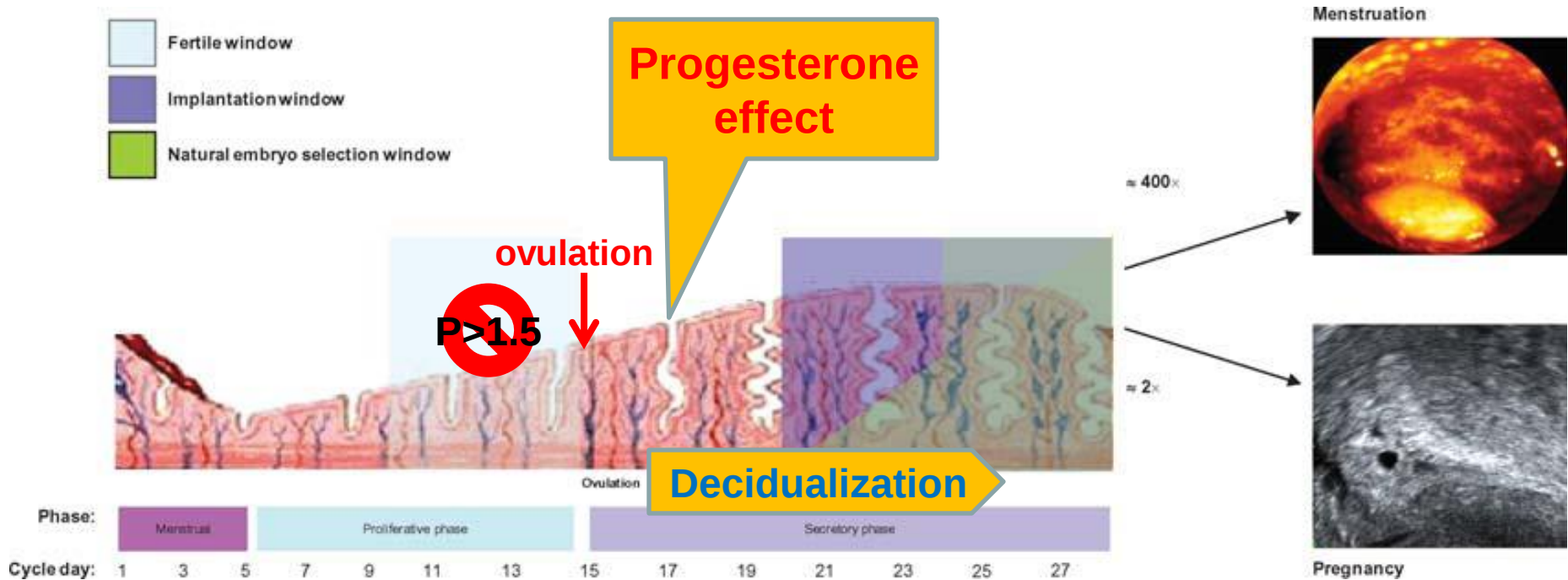
Ovidrel x 1.5支

Date	3/29	4/2	4/5	4/7	4/10	
Stimulation day						
E ₂ (pg/ml)	48.13	841	2994	取		
LH (mIU/ml)	5.16	3.72	3.37	取		
PGTR (ng/ml)	0.90	1.28	2.98	取		
Endometrial Thickness (mm)	6.8	4.1	9	①	ET	
βHCG=0.13 TSH=7.15 Follicular Size	Rt	R0 23x22	16x9	22x12	8#	
		RF x7	15x8	15x10		
			10x9	15x9		
			9x8	10x7		
			6x6	7x6		
	Lt	L0 30x15	13x10	19x16		
		LF x7	9x7	19x12		
			8x8	17x10		
			8x7	17x9		
			8x5	16x13		
			6x4	10x9		
			4x4	9x7 9x7		

☒ Check health list

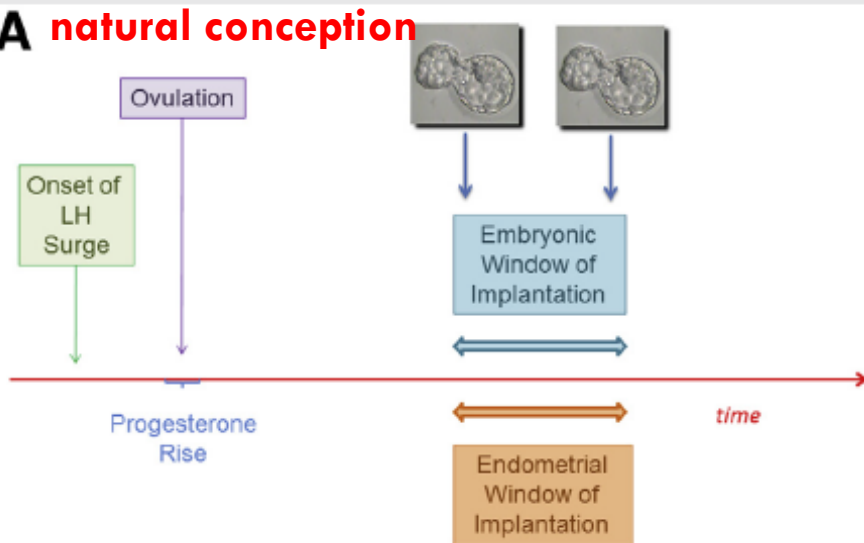
☒ Check ID 王前4支 101.03.29

Implantation Window

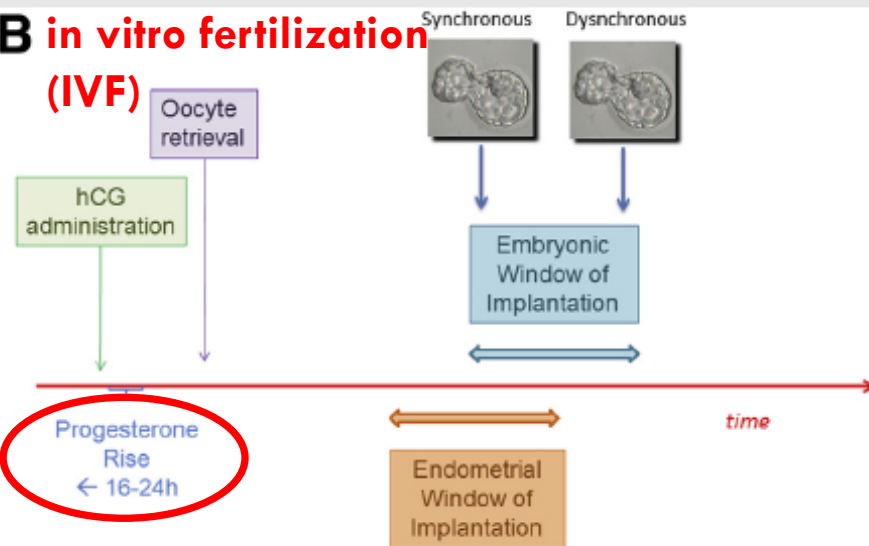


--Receptive to blastocyst implantation ~6 days after ovulation and remains receptive for 4 days.

A natural conception



B in vitro fertilization (IVF)



Embryo and endometrial synchrony involves both the endometrium, whose window is determined by the progesterone stimulus, and the embryo, whose window is relative to blastulation. (A) During natural conception, a rise in progesterone follows the luteinizing hormone surge and leads to the opening of the endometrial window of receptivity, which overlaps with the window of embryonic blastulation and implantation. (B) In in vitro fertilization, natural coordination can be lost. The rise in progesterone after the ovulation trigger is faster and more robust, and the progesterone stimulus shifts the endometrial window of receptivity by 16 to 24 hours. Additionally, blastulation may be delayed, particularly in older, low responders. These two factors, either alone or together, result in a physiologic dyssynchrony that cannot be predicted before the cycle start and may not necessarily be reproduced from cycle to cycle.

Franasiak. Endometrial and embryo dyssynchrony. Fertil Steril 2016.

□ A. Natural conception:

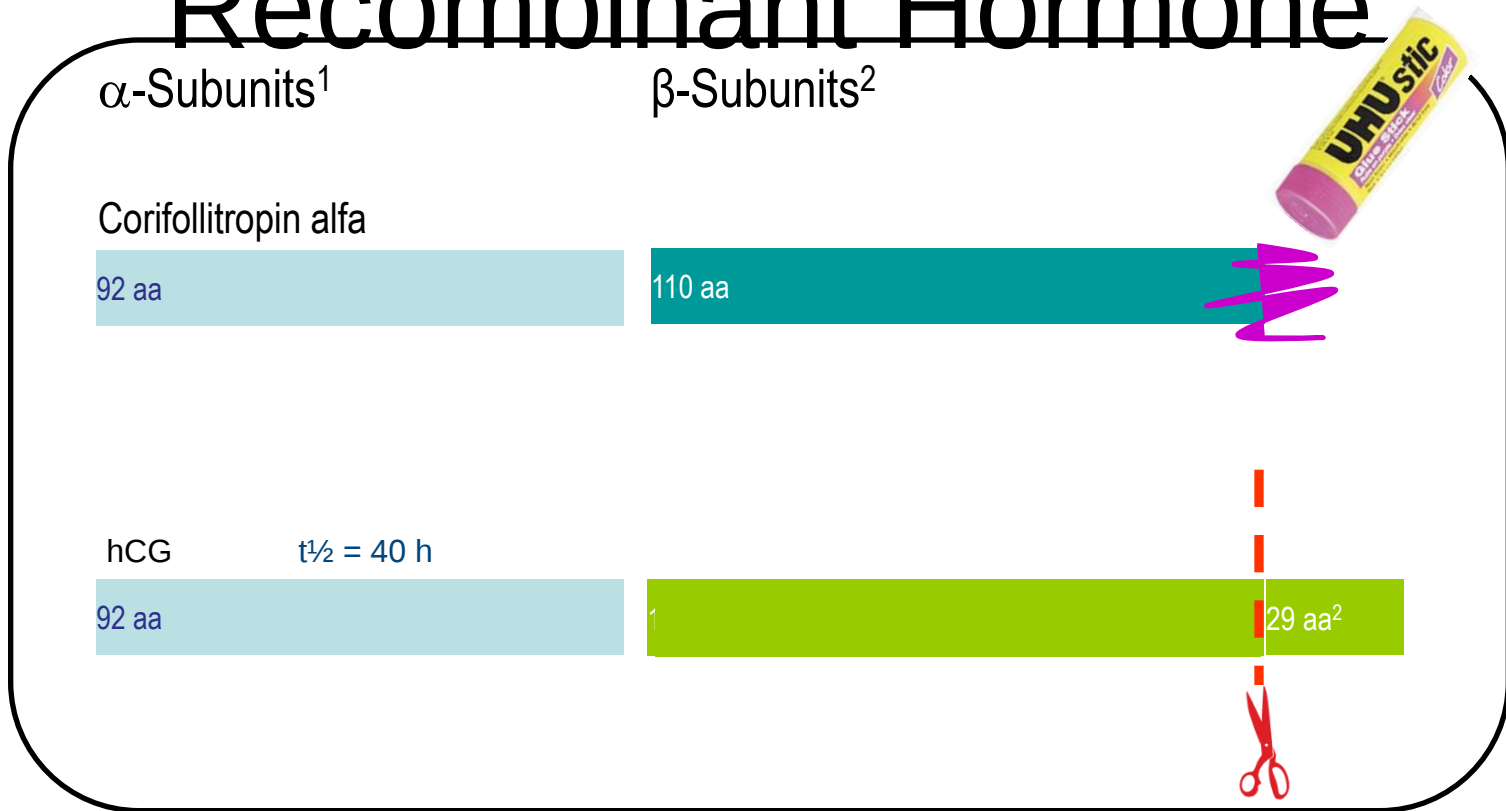
LH surge → ovulation → oocyte exposed to spermatozoa → embryonic window of implantation (WOI, blastulation)

meaningful P shortly after LH surge ↑ → secretory transformation → endometrial window of implantation (WOI)

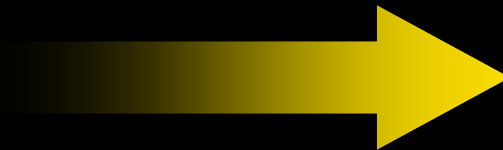
□ B. IVF (lost of natural coordination = embryonic-endometrial dyssynchrony):

- 1. P ↑ faster (16~24 hr)
- 2. blastulation may be delayed (older, low responders)

Corifollitropin alfa (Elonva®) Is a Recombinant Hormone



$t_{1/2}$ rFSH = 40 h³

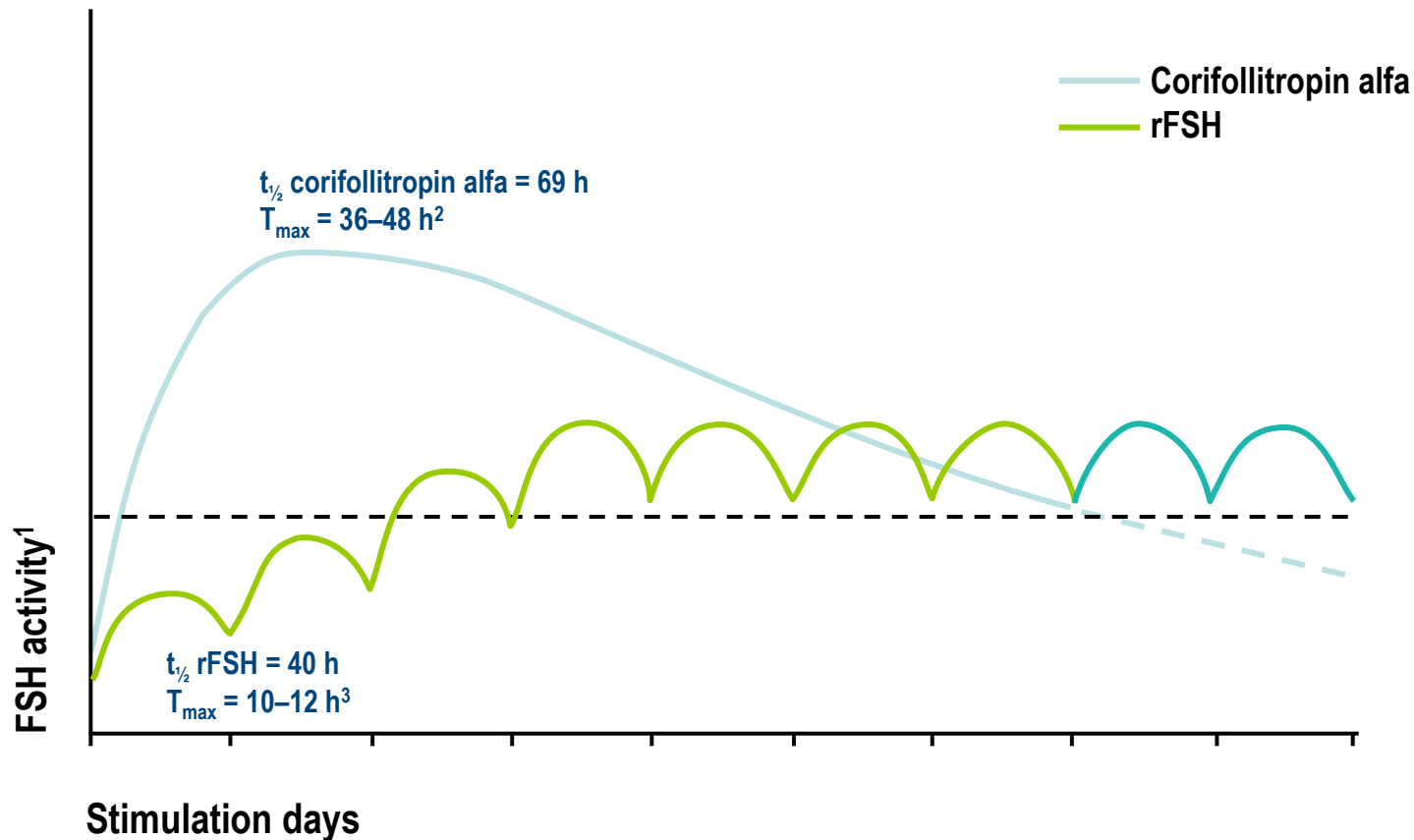


$t_{1/2}$ corifollitropin alfa = 69 h⁴

aa = amino acids; $t_{1/2}$ = half life.

1. Adapted with permission from Strauss J et al. Yen and Jaffe's *Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management*. 5th edition. Saunders; 2004; 2. Fares FA et al. *Proc Natl Acad Sci U S A*. 1992;89:4304–4308; 3. PUREGON® (rFSH) summary of product characteristics, 2010.; 4. ELONVA® (corifollitropin alfa) summary of product characteristics, 2010.

Comparative Pharmacokinetics



rFSH = recombinant FSH; $t_{1/2}$ = half-life; T_{max} = time to maximum concentration.

1. Adapted with permission from Fauser BC et al. *Hum Reprod Update*. 2009;15:309–321; 2. ELONVA® (corifollitropin alfa) summary of product characteristics, 2010;
3. PUREGON® (rFSH) summary of product characteristics, 2010.

Long protocol (GnRH agonist down-regulation protocol)

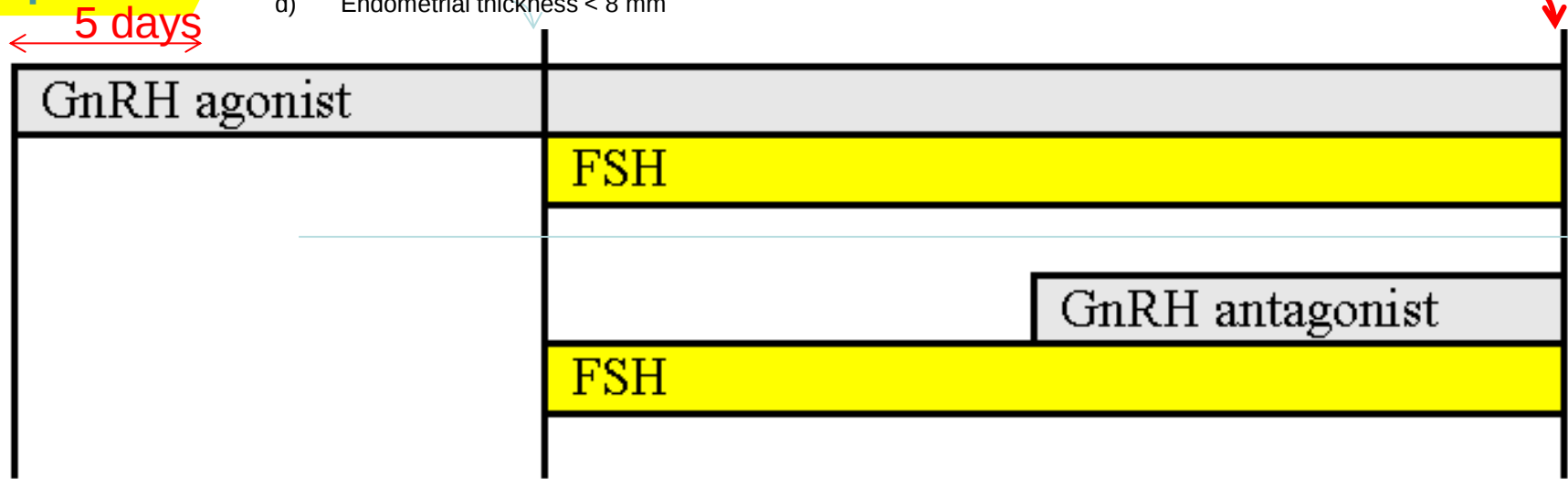
Dual suppression:

2-3 weeks of
(monophasic)
Oral pills

Monitoring of Pituitary down-regulation:

- a) Menstrual bleeding
- b) E2 < 80 pg/ml
- c) P4 < 1.5 ng/ml
- d) Endometrial thickness < 8 mm

Trigger: hCG



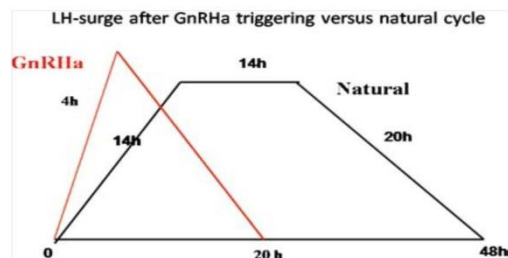
Mid-luteal phase
of previous cycle

Onset of stimulation

GnRH antagonist protocol

Trigger via hCG vs GnRHa

- hCG trigger → longer and stronger luteotropic activity
- GnRH agonist (GnRHa) trigger → more rapid luteolysis



Trigger: hCG
or GnRH agonist

Flare up
FSH & LH ↑
亦即
內生性LH surge
(幅度夠, 但duration略遜)
+
FSH surge (hCG trigger所缺)

Mens & OBS Hx : LMP 10-4-19 , PMP _____ , G _____ P _____ A _____ AA _____

Purpose : ☐ Ovulation induction/monitoring only ☐ AIH ☒ IVF/ICSI ☐ Other _____

Treatments ☒

月經週期		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
月/日		4/19	4/20	4/21	4/22	4/23	4/24	4/25	4/26	4/27	4/28						
核醫抽血檢驗					✓			✓	✓	✓							
濾泡超音波檢查					✓			✓	✓	✓							
Mercilon (美適儂)	口服																
Leuplin (柳菩林)	皮下; 午																
Cetrotide (欣得泰)	皮下; 午					0.25	0.25	0.25	0.25	0.25	0.25						
Menopur (美諾孕)	皮下; 上午	1x1 (1/1)		75	75	75	75	75	75	75	75						
Gonal-F (果納芬)	皮下; 午																
Puregon (保妊康)	皮下; 下午	pm6-9	225	225	225	225	225	225	225	225	225						
Pergoveris (倍孕力)	皮下; 午																

Antagonist protocol 搭配
Dual trigger:
GnRH agonist (Decapeptyl® 0.2 mg)
+ low-dose hCG (Pregnyl®)
[怕OHSS者hCG只給0~1500 IU]

Lab. Finding :

Date	4/20	4/27	4/28	4/29	4/28	4/30
Stimulation day						
E ₂ (pg/ml)	30.62	651	1633	470	702	702
LH (mIU/ml)	3.80	1.25	1.23	3.23	4.9	4.9
PGTR (ng/ml)	0.58	0.43	0.74	1.05		
Endometrial Thickness (mm)	8.8	14.1	19.8	20.5		(2)
FSH= 4.90 hCG=0.10 <						

☒ Check health list 101.04.24 ☒ Check ID 陳美如 101.04.20 107 7x6 7x9 6x6

Mens & OBS Hx : LMP 10.3.09 08 , PMP , G 2 P 1 A 1 AA

Purpose : ☐ Ovulation induction/monitoring only ☐ AIH ☒ IVF/ICSI ☐ Other

Treatments 50kg

月經週期	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
月/日	9/8	9/9	9/10	9/11	9/12	9/13	9/14	9/15	9/16	9/17	9/18	9/19				
核醫抽血檢驗					✓			✓	✓	✓						
濾泡超音波檢查					✓			✓	電	✓						
Mercilon (美適儂)	口服															
Leuplin (柳菩林)	皮下; 午															
Cetrotide (欣得泰)	皮下; 上午	1支 + 1粉						1支	1支	1支	1支					
Gonal-F (果納芬)	皮下; 午	150	150	150	150	150	150	150	150	150	75					
Decapeptyl (德卡普提)	皮下; 午	0.2			75	75	75	75	75	75						

Antagonist protocol 搭配
Dual trigger 亦可用於不怕OHSS者:
6500 IU hCG (Ovidrel® 一支) +
GnRH agonist (Decapeptyl® 0.2 mg)
[取其FSH surge的好處]

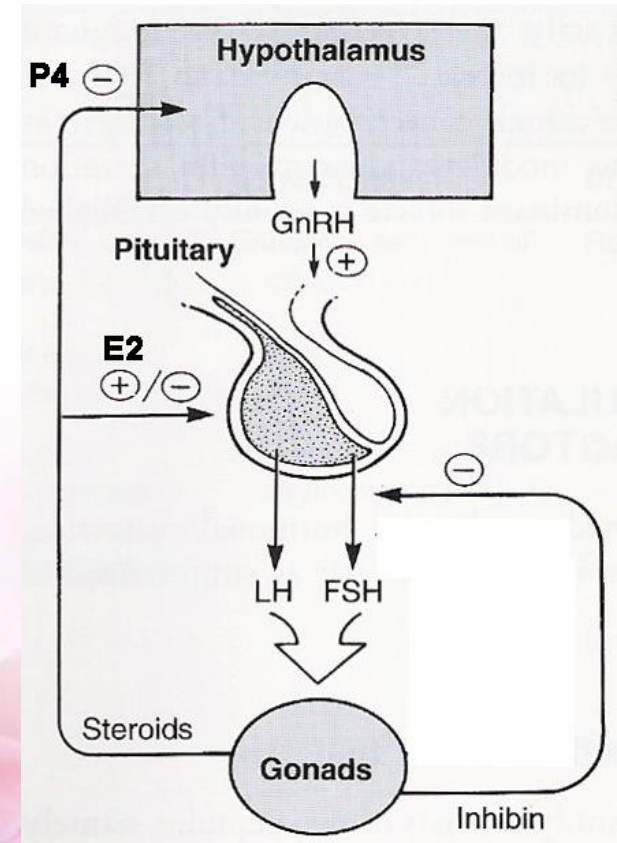
Decapeptyl + Ovidrel

Date	9/9	9/12	9/15	9/16	9/17	9/19
Stimulation day						
E ₂ (pg/ml)	32.0	293.0	1071.0	1758.0	2052.0	
LH (mIU/ml)	3.98	1.1	1.01	1.41	2.20	
PGTR (ng/ml)	0.4	0.3	0.4	0.4	0.6	ET
Endometrial Thickness (mm)	6.8	8.4	11.6		13.4	9.0
Follicular Size	Rt	cos 26x18	10x9 9x5	17x13 13x7	22x13 15x12	5 #
		RF 15x15	10x8 8x6	17x12 12x12	24x13 15x12	
			9x9 8x6	16x14 12x9	20x14 14x11	
			9x7 8x5	15x14 11x8	18x16 13x9	
			9x6 7x6	15x13 10x5	18x15	
			9x6 7x6	15x13	18x11	
	Lt	LF 12x12	12x8 7x5	17x13 11x9	21x13 13x10	22 ET
			11x8 7x5	16x13 11x8	19x16 12x11	
			10x7 6x4	15x14	18x10 4x7	
			9x7	15x11	17x15 9x6	
			8x7	14x9	17x13	
			8x6	12x9	17x10	
ET 110217		7x5	12x8	16x13		

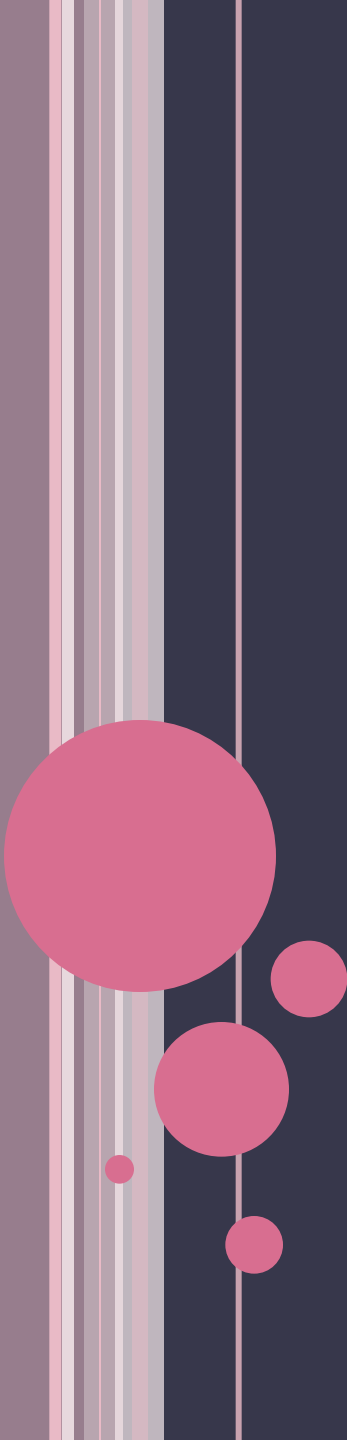
Use of progestogen to block LH surge

- The LH surge is caused by the increase in plasma E2 at the end of the follicular phase
- Studies on contraception have shown that **progesterone is able to block this LH surge and therefore ovulation**
- Experiments on monkeys have shown that
 - The administration of a progestin (levonorgestrel) at the beginning of the cycle prevents the LH surge despite the increase in E2, for as long as it is continued
 - The inhibition of the LH surge by progesterone is a **hypothalamic** action

(Massin N, Hum. Reprod. Update, 2017)



OVARIAN STIMULATION FOR IVF/ICSI



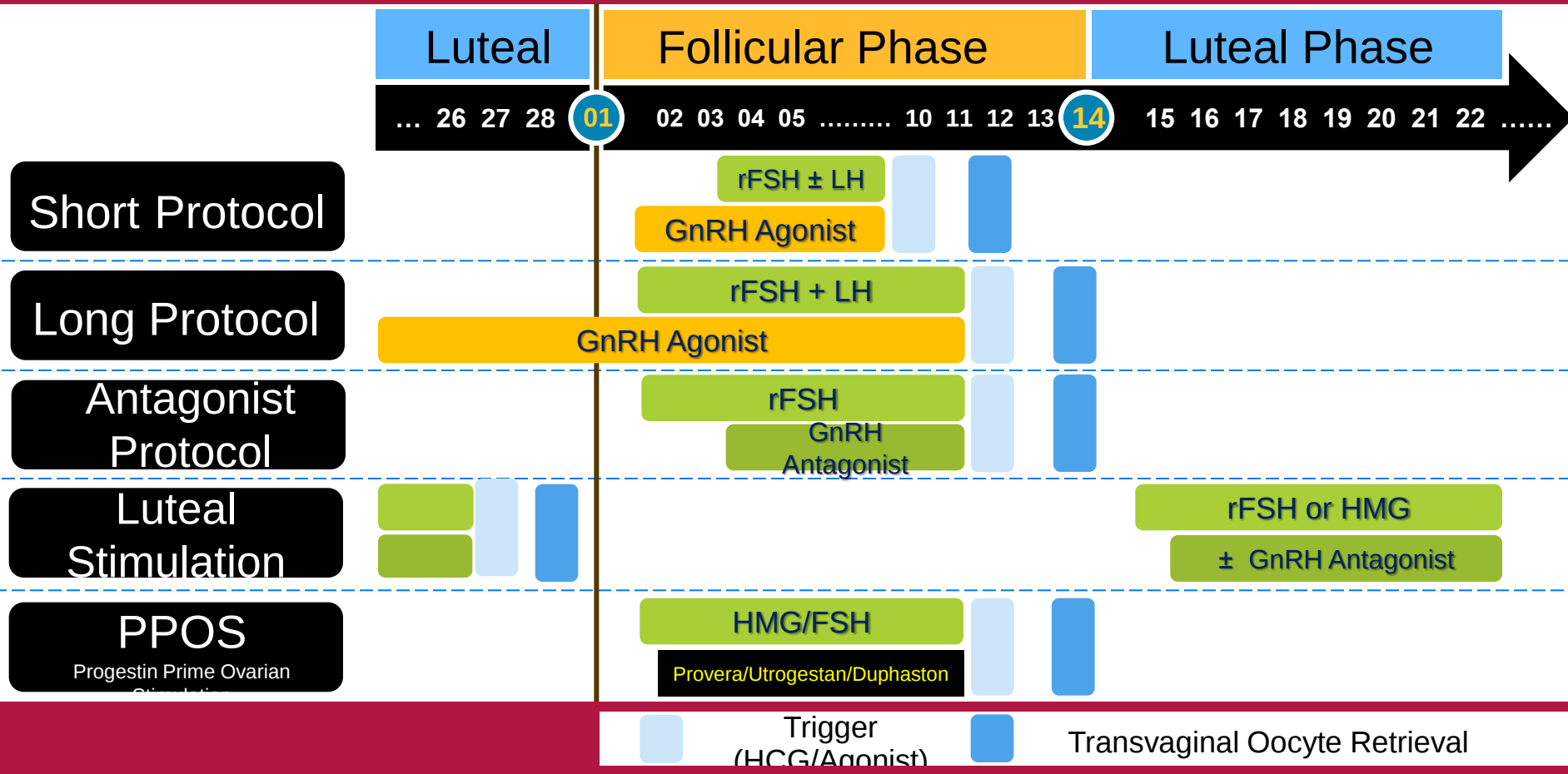
Gonadotropin for
follicle development



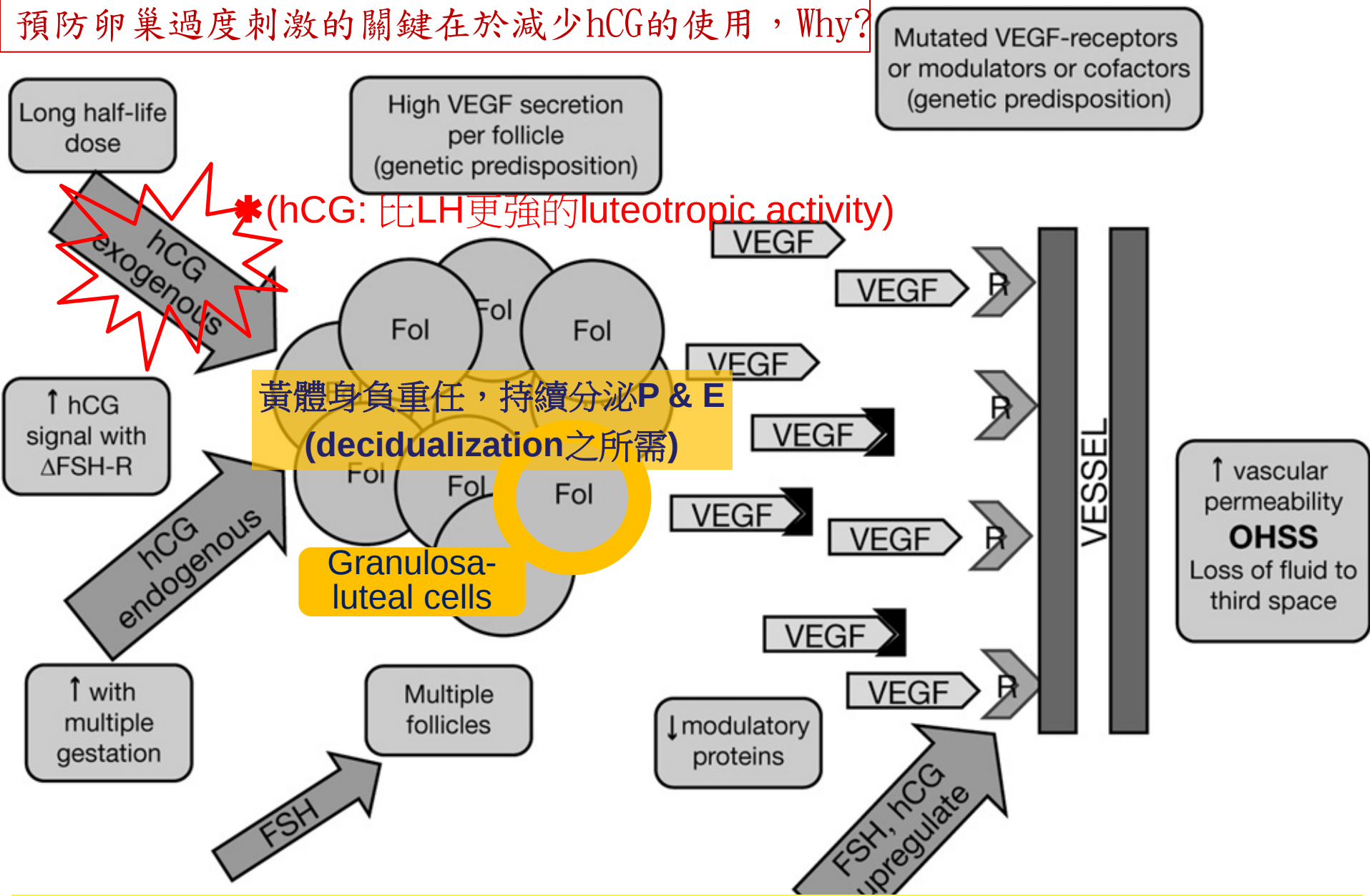
Exogenous P

Prevent LH
premature surge

Different IVF Protocols



預防卵巢過度刺激的關鍵在於減少hCG的使用，Why?

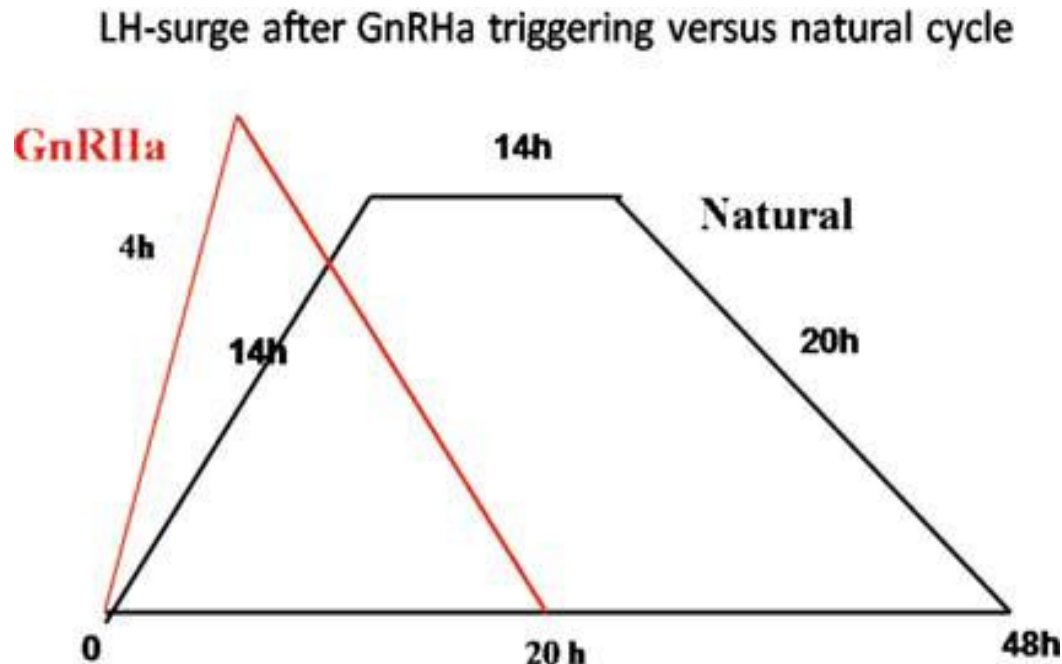


黃體愈旺(luteotropic activity ↑ ↑)=著床愈穩但OHSS可能愈嚴重

(Humaidan. Prevention strategies for OHSS. Fertil Steril)

Trigger via hCG vs GnRHa

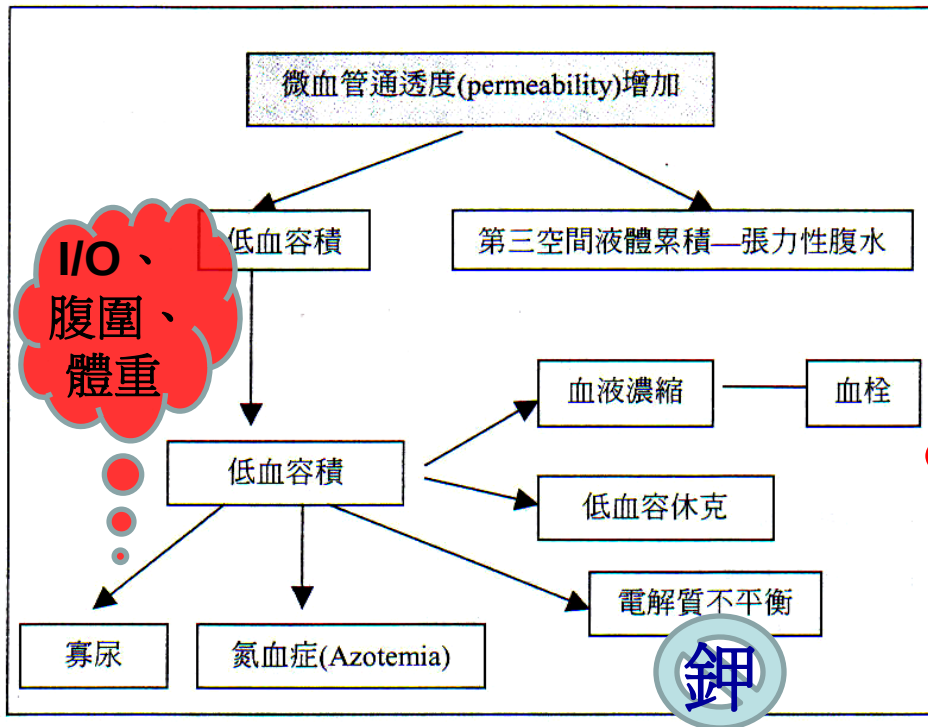
- hCG trigger → longer and stronger luteotropic activity
- GnRH agonist (GnRHa) trigger → more rapid luteolysis



不孕症治療常見之併發症

- 卵巢過度刺激症候群 OHSS

嚴重 OHSS 的病生理變化



1. 嚴重度分類

	輕中度	嚴重	危急
Enlarged ovary	5-12 cm	>12 cm	various
腹脹	中度	嚴重	緊繃
胸腔積水(Hydrothorax)	-	有	量多
腎功能衰竭	-	-	+/-
血栓疾病(Thromboembolic disease)	-	-	+/-
ARDS(成人呼吸窘迫症)	-	-	+/-
Hct (%)	<45	≥45	≥55
WBC	<15000	≥15000	≥25000
肝功能(轉氨酶)變化	正常	上升	上升
Cratinin (ng/mL)	<1.0	1.0-1.5	≥1.6
CCr (mL/min)	>100	50-100	<50

可預測誰會發生卵巢過度刺激症候群嗎？

-probably not

- ~~Higher androgen levels (Elder-Geva 2005)~~
- ~~Higher AMH levels (Kaya 2010)—broad range~~
- ~~Higher insulin (Fulghesu 1997)— others suggesting greater gonadotropin dose requirement (Homburg 1996)~~
- No good way except prior history
- 就算沒有危險因子仍可能潛在過度刺激的風險
- 每個多囊患者接受排卵針都有風險
- 只要有多囊型態的卵巢，無論是否符合多囊性卵巢症候群的診斷標準，風險一樣高！ (Kim YJ 2010; Swanton A 2010)

C有關卵巢過度刺激症候群（OHSS）的敘述，下列何者錯誤？

A卵巢會腫大

B嚴重時會有腹水

C通常需要以剖腹探查來治療

D臨床症狀通常在人類絨毛膜促性腺激素（hCG）注射後3—7 天開始出現

A.一位28 歲不孕症婦女在6 天前接受取卵手術，共取出20 顆卵子，2 天後植入3 個胚胎。今天來到急診，主訴呼吸困難、腹脹以及噁心。超音波發現兩側卵巢腫大約6 公分、有大量腹水。下列那一項處置較不適合？

A抽血驗CA125, CEA, CA199

B抽血驗CBC, electrolytes, GPT(ALT), BUN, creatinine

C抽腹水

D給予大量normal saline

Oocyte retrieval (Egg pick up)

取卵

Timing of Oocyte Retrieval

- Scheduled at about 34-36 h after hCG injection: the oocytes are expected to ovulate at 37 h post-hCG.
- After hCG injection, the intercellular connections between the granulosa cells and the oocytes are interrupted
- Meiosis is resumed and the oocyte progresses from prophase I to metaphase II.

103年第一次專技高考

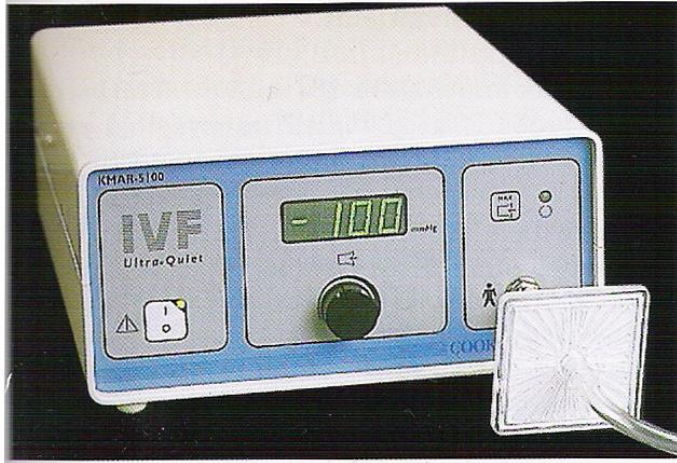
醫師二醫學六

* 取卵的時機一般是在絨毛性腺激素
(human chorionic gonadotropin) 注射後幾
小時？

- A. 20~24 hr
- B. 34~36 hr
- C. 40~44 hr
- D. 48~52 hr

B

Preparation of Materials for Oocyte Retrieval

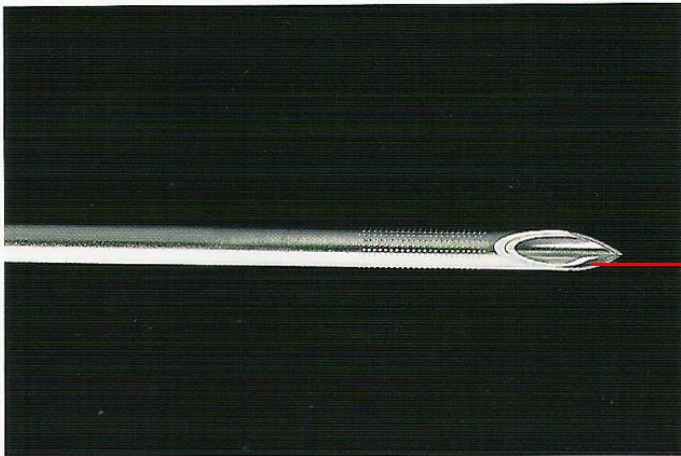


Aspiration Unit



Falcon tube heater

1. Place the test tubes, handling medium, and thermometer in a warm block on the staging stage
2. Flush the aspiration needle and its tubing with medium.
3. Single lumen v.s. double lumen needle
(The dead space of the needle and tubing is about 1 ml)



Echo Tipping

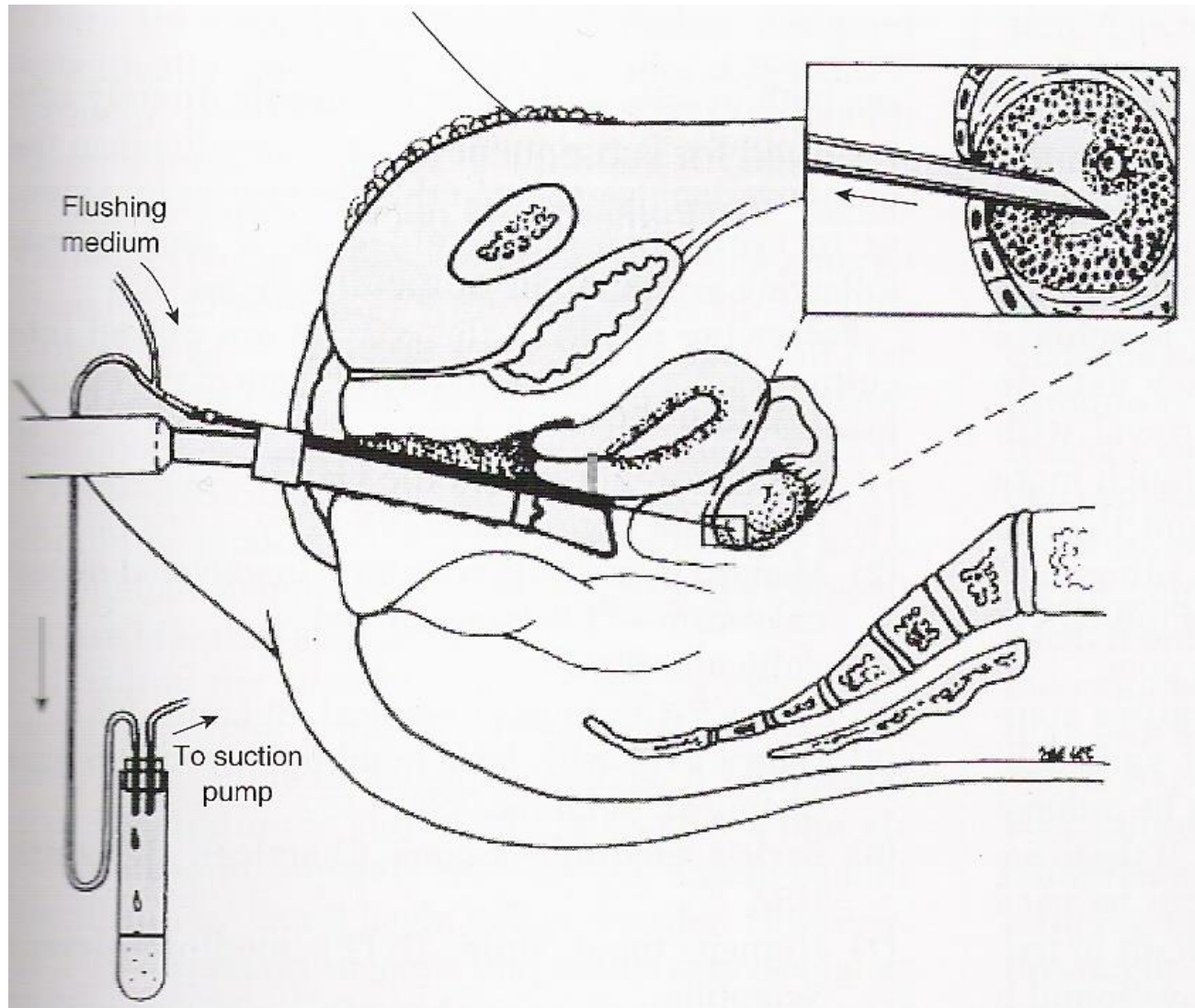
Ovum Pick-up Needle

(Textbook of ART, 2nd Ed., 2004)

手術全程保持無菌狀態,並在超音波導引下進行取卵

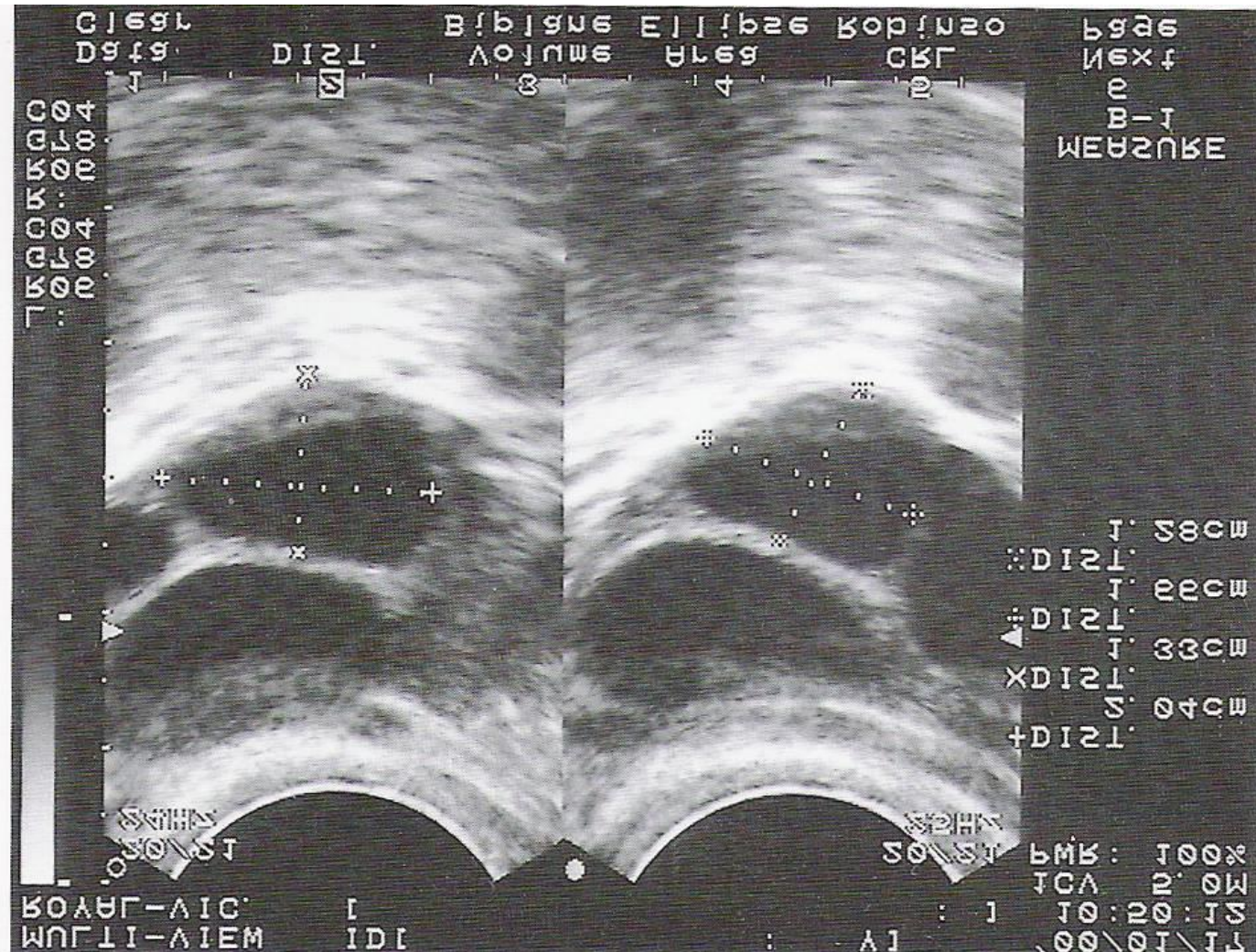


經陰道以超音波輔助取卵



(Textbook of ART, 2nd Ed., 2004)

經陰道以超音波輔助取卵



取得卵子顯微鏡下結構

卵丘卵子複合體 →

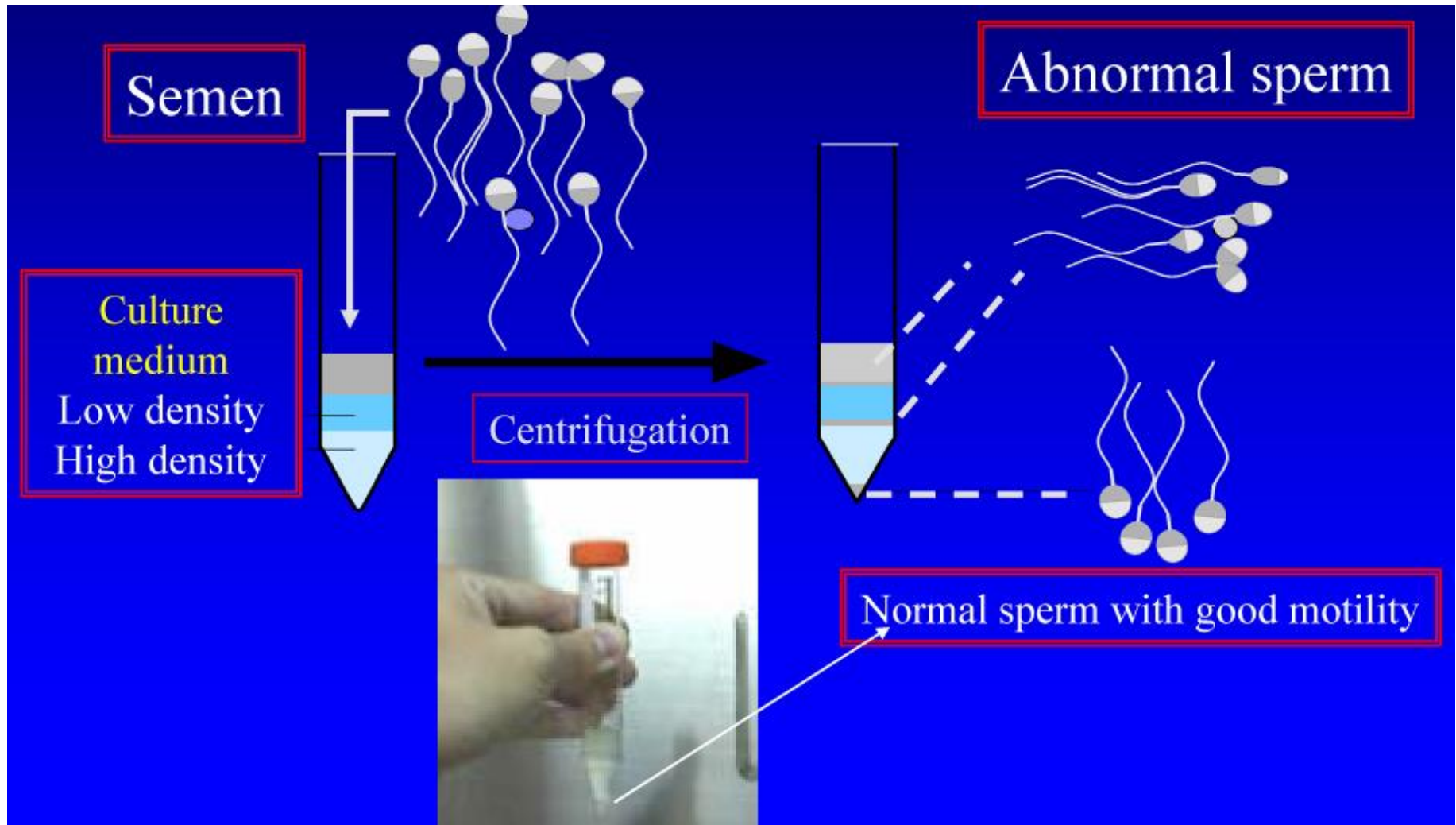


不成熟卵子

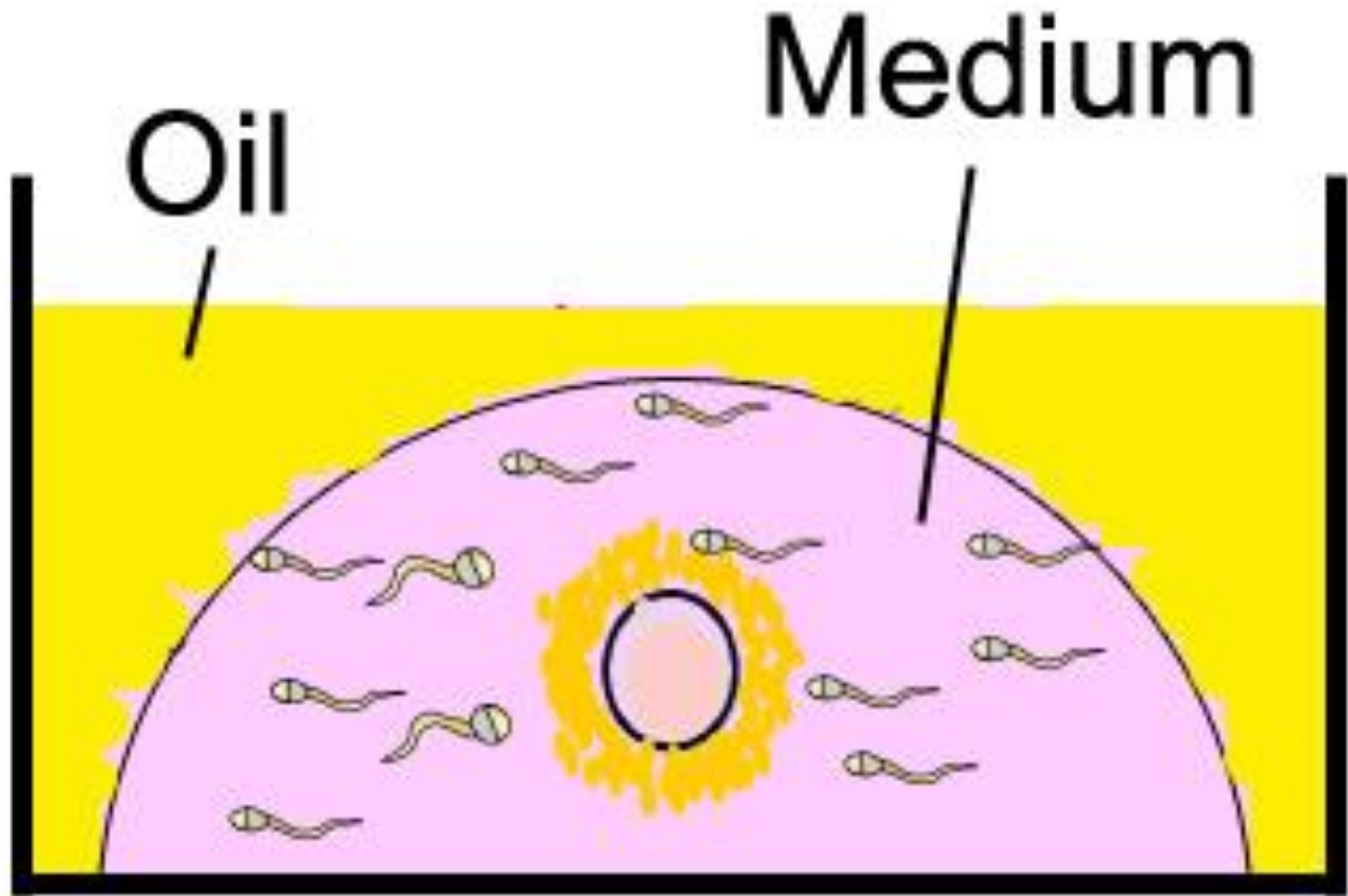


成熟卵子

精蟲之準備

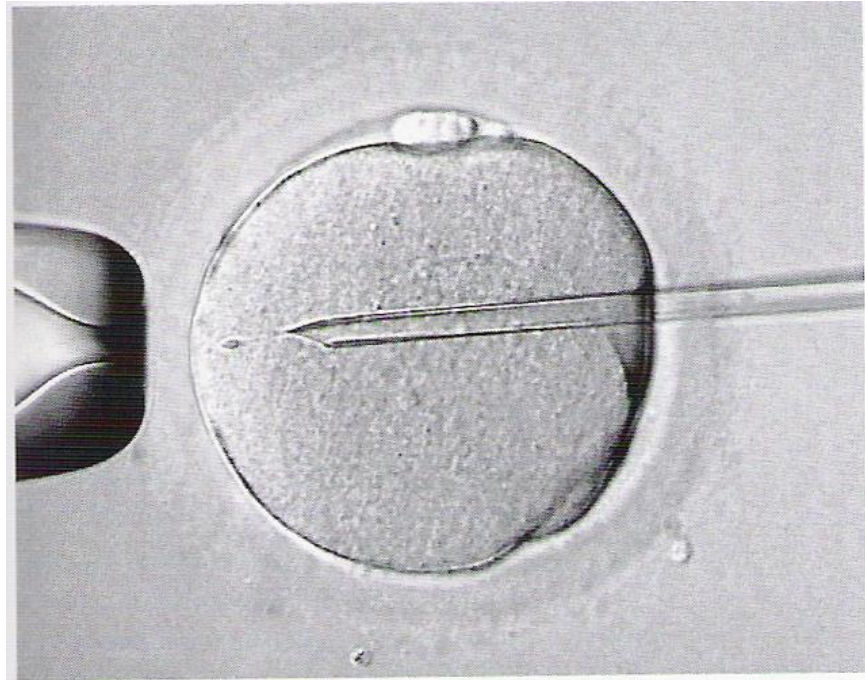
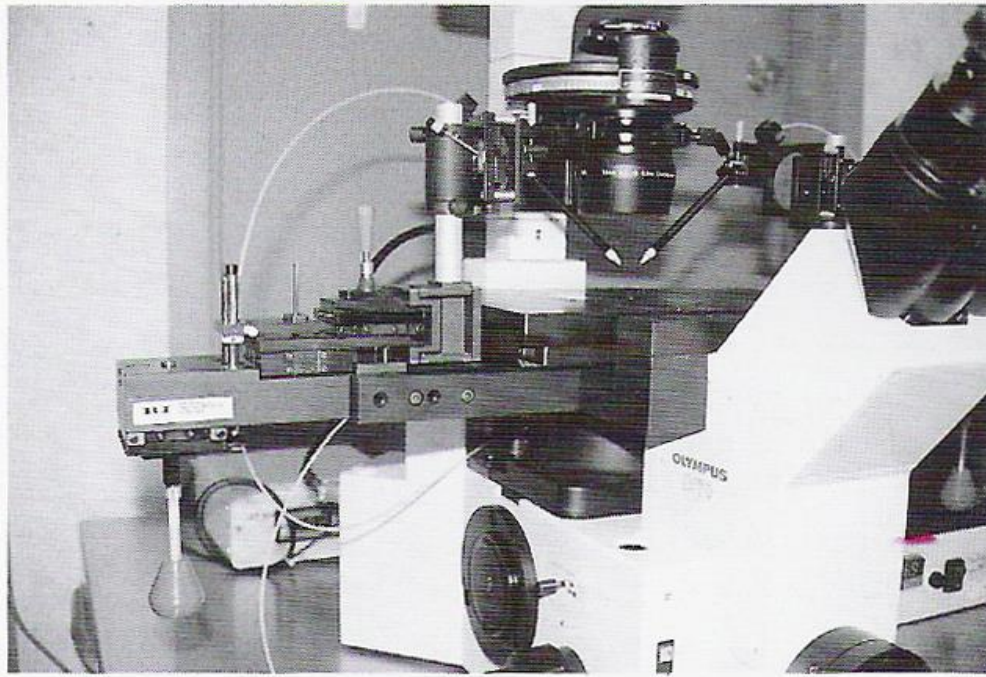


卵子體外受精 (*in vitro* fertilization)



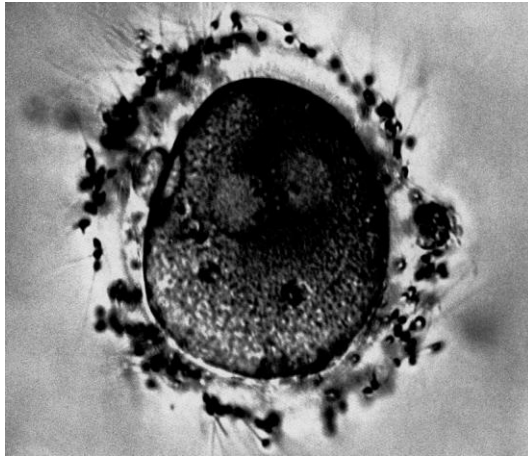
精蟲顯微注射：(ICSI)

應用在合併男性不孕或先前嘗試受精率低者

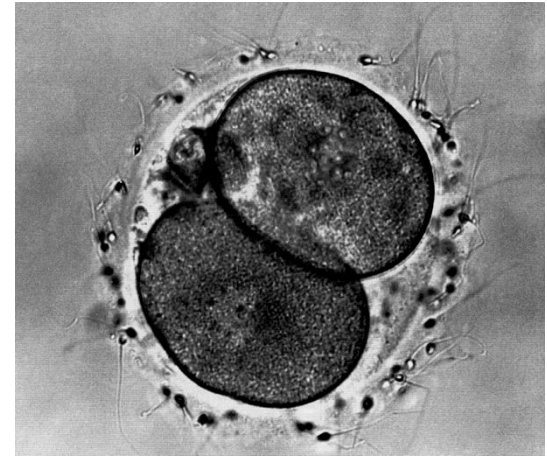


體外受精及胚胎早期發育

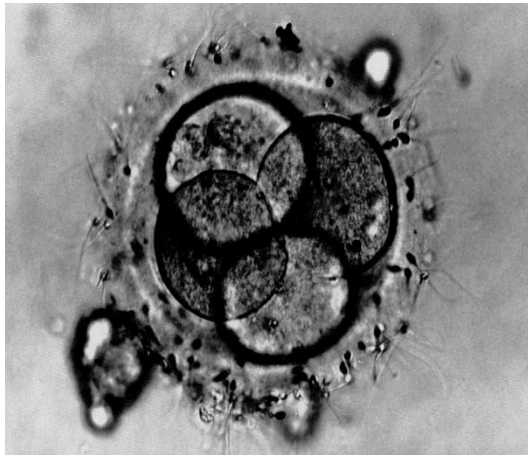
受精卵



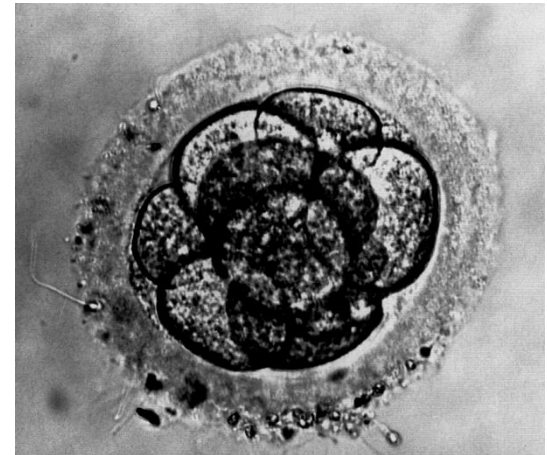
兩細胞



八細胞



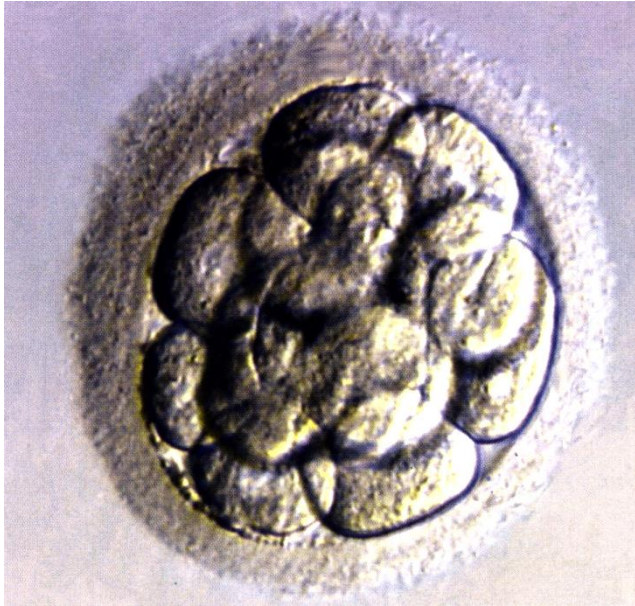
四細胞



D3植入
或
繼續培養

胚胎培養至囊胚期

桑葚胚

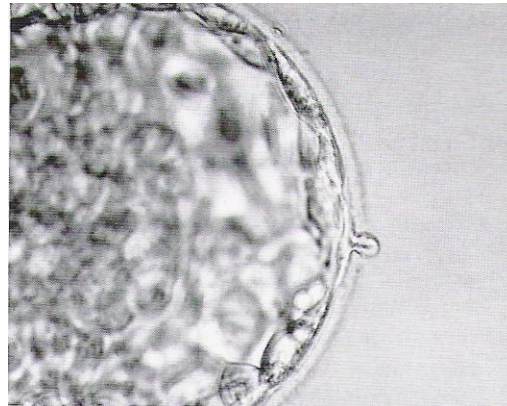


囊胚



D5植入

雷射輔助孵化 →



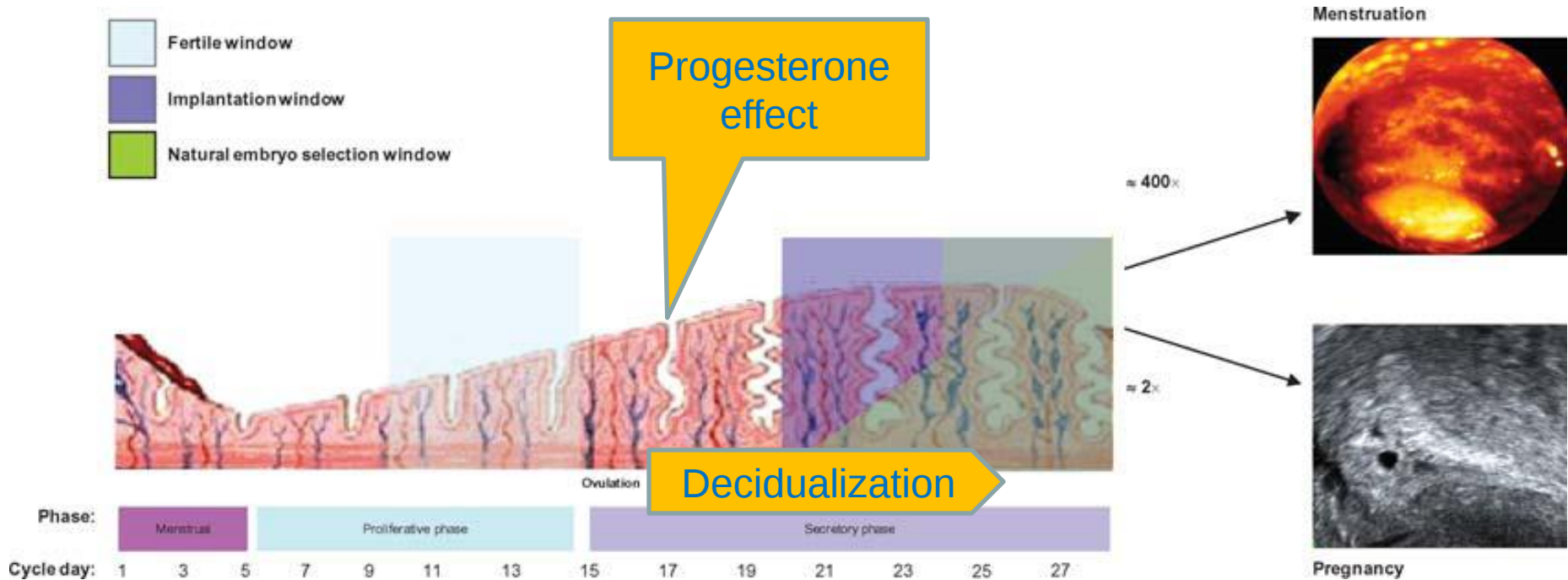
黃體期補充

人工生殖中為何要黃體期補充？

Abnormal Luteal Function After Ovarian Stimulation for IVF: Mechanisms

- Continued down-regulation by GnRHa
→ LH ↓
- Induction of multiple follicles *per se*
- Removal of large quantities of granulosa cells at oocyte retrieval
- Supraphysiological E2/P4 in early luteal phase → negative feedback → LH ↓

Implantation Window



--Receptive to blastocyst implantation ~6 days after ovulation and remains receptive for 4 days.

Elements of Luteal Phase Support

- HCG: 1500-2000 IU i.m. q3d for 4 doses from oocyte retrieval
- P4: from oocyte retrieval to 7-10 weeks
 - 1) progesterone in oil 25-100 mg i.m. qd
 - 2) utrogestan 200 mg p.o. or vag. tid-qid
 - 3) Crinone gel 90 mg vag. qd
- E2: from oocyte retrieval to 7-10 weeks
E2 valerate 2 mg p.o. bid

破卵

34~36小時
之後

取卵

術後用藥

+

Luteal support
(藥物+monitor)

.. 破卵針 (Decapeptyl + Pregnyl):

- 1) 買藥地點: 健康人生藥局, 須在晚上 9 PM 前
- 2) 藥品運送及保存方式: 須放在冰塊上攜帶, 回家放置冰箱冷藏而非冷凍
- 3) 接受注射地點: 中正 8F 產房, 請攜帶此單
- 4) 注射時間: 101 年 4 月 7 日 晚上 9 時 30 分 (21:30 PM)
- 5) 注射劑量及途徑: Decapeptyl 0.2 mg (0.1 mg/支 x 2 支), sc 皮下注射 (左下腹 1 支, 右下腹 1 支) + Pregnyl (HCG) 1500 IU, im 肌肉注射 (1 瓶注射水溶解 1 瓶 1500 IU 藥粉, 抽出 全部 份量, 臀部肌肉注射)
- 6) 抽血 (E2, LH): 101 年 4 月 8 日 早上 8:00-8:45, 中正 8F 生殖醫學中心, 下午 4-5 時諮詢師

.. 取卵:

- 1) 前一天晚上 12 點後禁食: 手術前 8 小時不吃東西、不喝水
- 2) 取卵報到地點及時間: 中正 8F 生殖醫學中心等候區, 101 年 4 月 9 日 早上 7 時 30 分 (7:30 AM) 報到, 交 Notes (1000 mg/支, 室溫儲存) 1 支給護士; 手術後護士會向家屬取 progesterone (25 mg/支, 室溫儲存) 2 支
- 3) 取卵風險包括細菌感染、內出血、及腸子等臟器受損, 若有劇烈腹痛、發燒、心悸、頭暈等不適, 請至本院急診就醫

.. 取卵後使用藥物: 以下藥物均為取卵後才開始使用

- 1) Lopilexin 口服, 每日四次, 每次一粒, 取卵後服用三天
- 2) Mag. oxide 口服, 每日四次, 每次一粒, 取卵後服用三天
- 3) Scanol 口服, 每日四次, 每次一粒, 取卵後服用一天
- 4) Estrade 口服, 每日三次, 每次一粒, 取卵後天天吃; 自 101 年 4 月 12 日 起每日四次, 每次一粒, 直到驗孕。(取卵當日只吃兩次, 即日下午及睡前各一粒)
- 5) Progesterone 50 mg (25 mg x 2 支) im 肌肉注射, 取卵後天天注射; 自 101 年 4 月 12 日 起每日注射 100 mg (25 mg x 4 支), 直到驗孕。(取卵後於恢復室只注射 50 mg, 即 2 支)。(Progesterone 儲存於室溫陰涼處)
- 6) Dostinex 口服每晚一次, 每次一粒, 取卵後每天晚上吃, 直到驗孕。
- 7) Tapal 口服每早一次, 每次一粒, 取卵後一天 (即 4 月 10 日) 起每天早上吃, 直到驗孕 (須注意無下腹劇痛、頭暈、心悸等內出血現象方可服用)。

取卵後抽血: 上午 8:45 AM 前, 中正 8F 生殖醫學中心 (週一至週五) 或思源一樓核子醫學部 (週六); 下午 4:00~5:00 PM 打電話給諮詢師問報告, 以調整藥物劑量

1) E2, PGTR: 4 月 12 日、4 月 14 日、4 月 16 日

2) Beta-HCG, E2, PGTR: 4 月 23 日、 月 日

Dr. 李 0968898656

胚胎植入: 請於 4 月 10 日 下午 4:00~5:00 PM 打電話給諮詢師確定植入時間, 植入當日請上午 8:30 AM 至中正 8F 生殖醫學中心報到, 並攜帶兩個黏貼式成人紙尿褲。

電話: 請先打 0966285155 (蔡淑娟諮詢師); 蔡諮詢師請假時請打 0966287980 (林雅琇諮詢師)

3. 取卵後使用藥物：以下藥物均為取卵後才開始使用，

- 1) Lopilexin 口服，每日四次，每次一粒，取卵後服用三天
- 2) Mag. oxide 口服，每日四次，每次一粒，取卵後服用三天
- 3) Scanol 口服，每日四次，每次一粒，取卵後服用一天
- 4) Estrade 口服，每日三次，每次一粒，取卵後天天吃，直到驗孕。(取卵當日只吃兩次，即下午及睡前)
- 5) Crinone 塞陰道，取卵後一天(即12月22日)起每天早上塞一支，直到驗孕(Crinone 須冷藏)
- 6) Utrogestan 塞陰道，取卵後一天(即12月22日)起每天下午及睡前各塞一次，每次塞兩粒，直到驗孕
- 7) Tapal 口服每早一次，每次一粒，取卵後一天(即12月22日)起每天早上吃，直到驗孕(須注意無下腹劇痛、頭暈、心悸等內出血現象方可服用)。
- X 8) Pregnyl 1500 IU (1 水+1 粉，抽出全部份量)，im 肌肉注射，於_____、_____、及_____。

Micronized progesterone capsule



(



Intramuscular progesterone

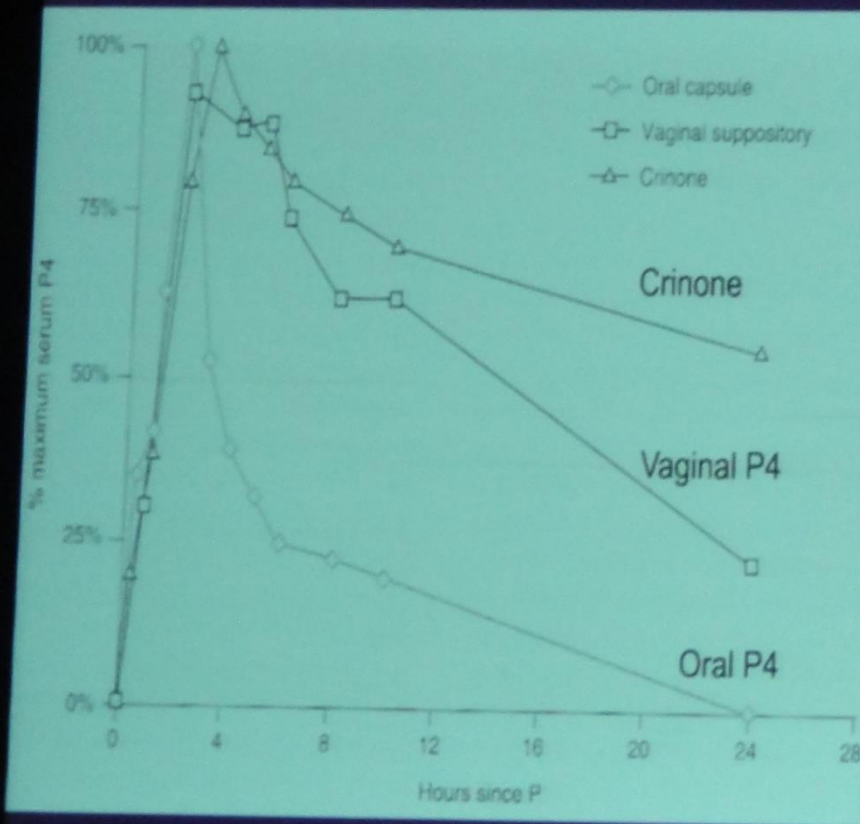


HCG

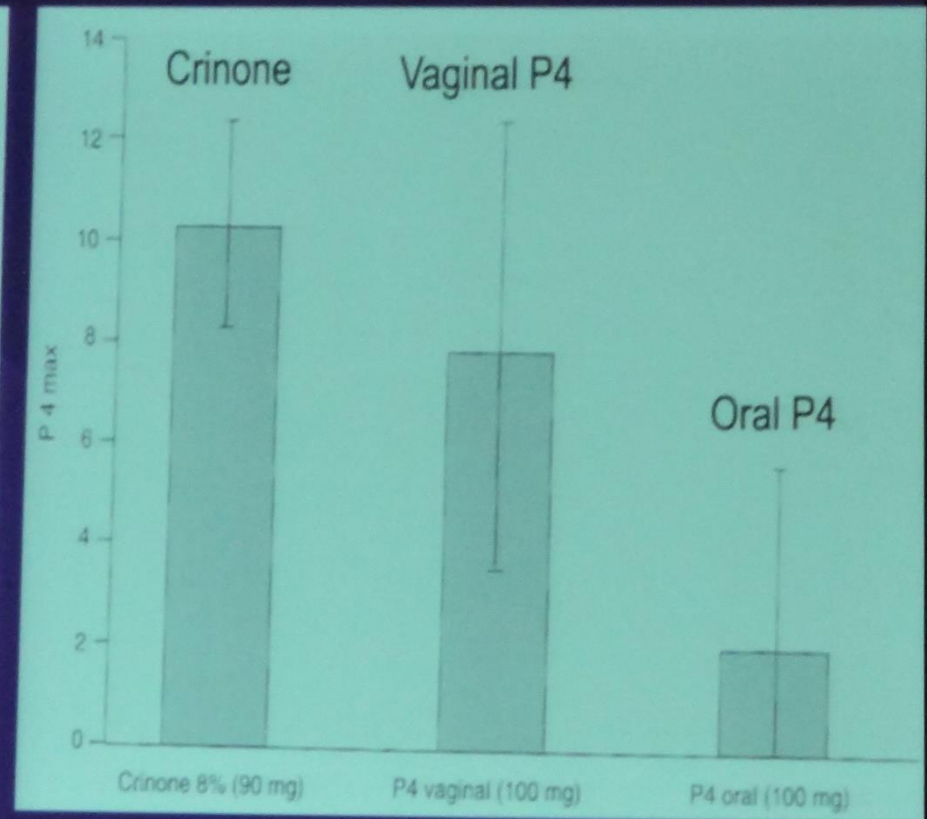


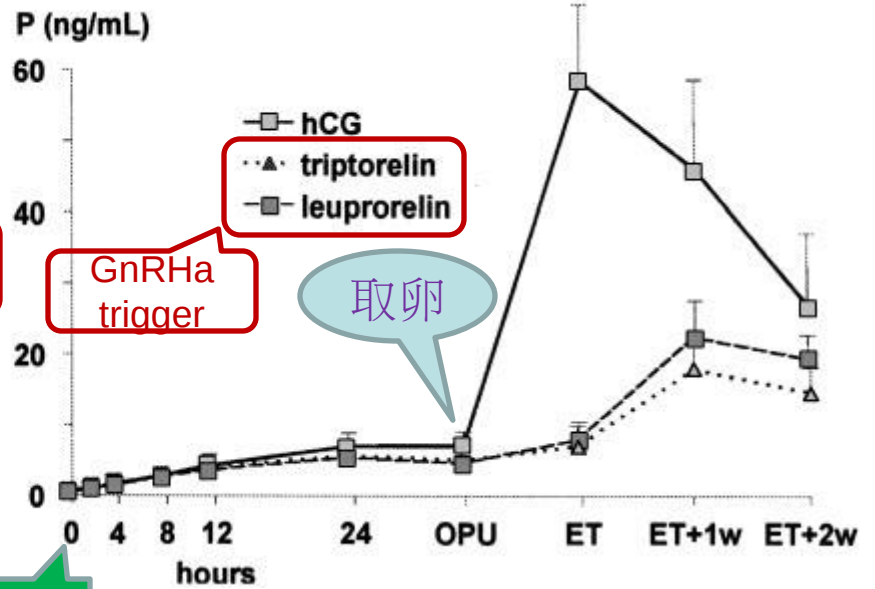
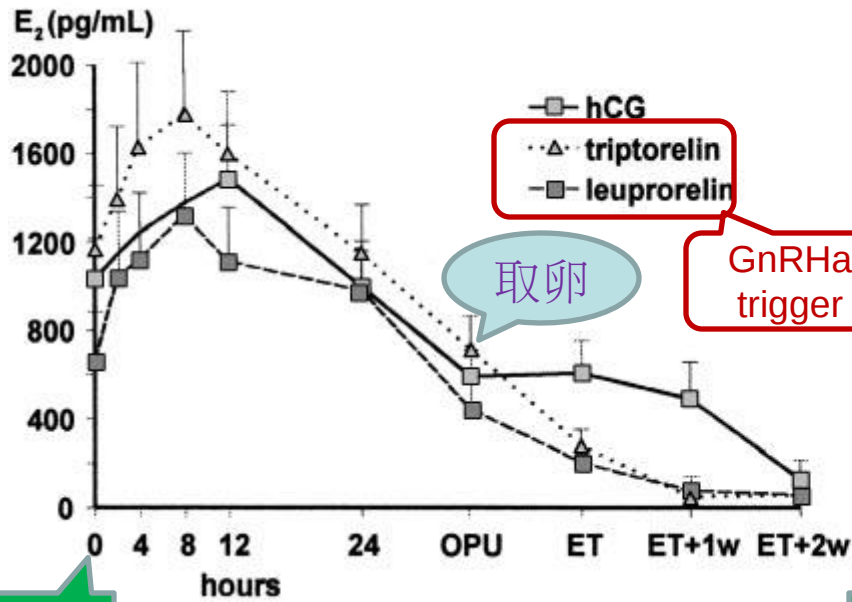
Crinone vs. Vaginal P4 vs. Oral P4

Longer half life



Lower pt. to pt. variability





ART誘導排卵後 黃體期之E與P

人工生殖技術療程取卵後追蹤

姓名: 林佩蓉 病歷號: 3895698-8 電話: 0982600630
0982400087

破卵日 E2: 4855 (4/6) 濾泡數 (≥ 10 mm): 21 #

取卵日: 4/9 取卵數: 12 #

胚胎植入日 (D3): 4/12 (提醒按照原來劑量繼續每天塞藥及吃藥)

植入當天早上塞藥及吃藥後再來報到, 早上 8:30 中正 8F 生殖醫學中心)

**提醒按照原來劑量繼續每天 ^{打針} 塞藥及吃藥 → Dr. 李

日期 (D ₃)	4/12 (D ₃)	4/14 (D ₅)	4/16 (D ₇)	4/23 (D ₁₄)
E2	2581	1464	2079	870
PGTR	161	120	181	64.8
Beta-HCG				2.07
處置	打針. 吃藥	Pregnyl 300 IU or Start	打針. 吃藥	打針. 吃藥

日期 (D ₃)	4/25 (D ₁₆)			
E2	✓ 766			
PGTR	✓ 107			
Beta-HCG	✓ 5.99			
處置				

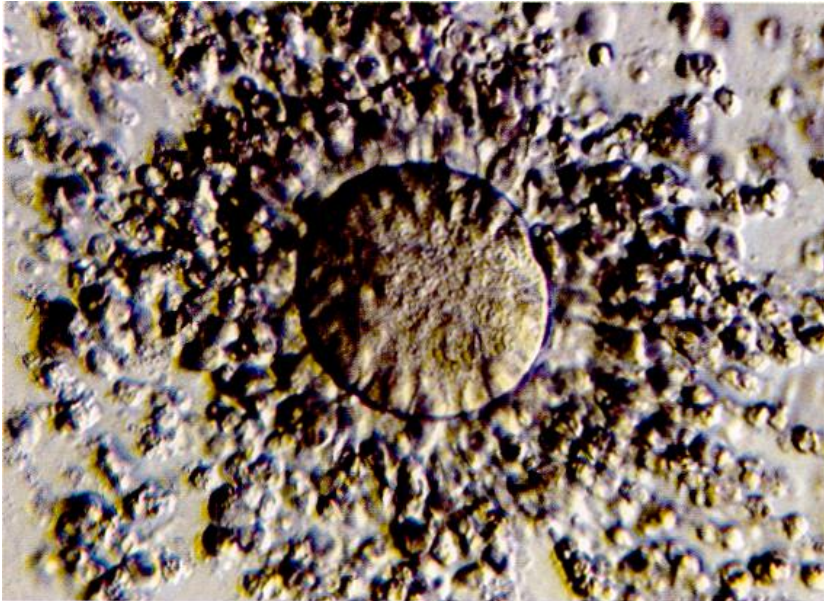
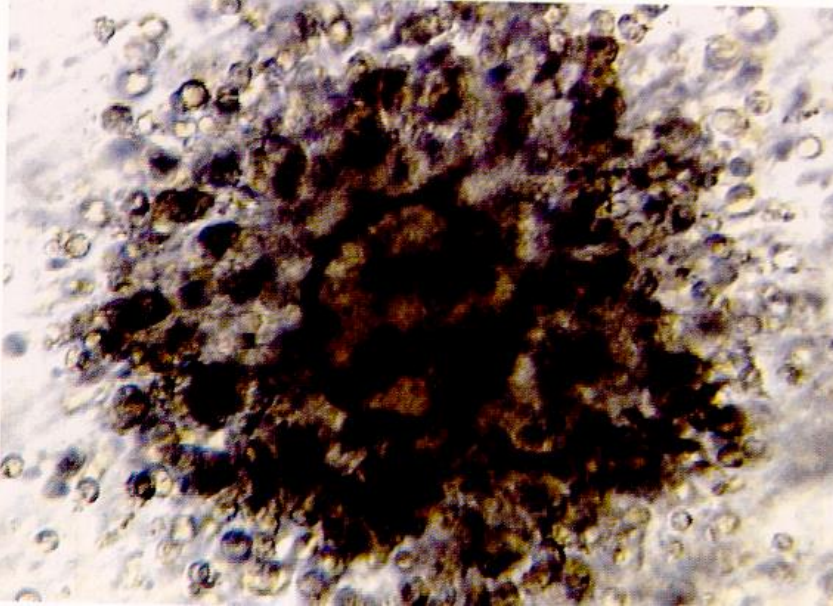
Dr. signature : Operator Dr. 莫曼 ; Recorder Dr. 3012

Sperm recovery : ☒ by patient ; ☐ by andrologist (☐ EEJ ☐ Epididymis ☐ Testis)
Sperm preparations : ☒ Swim up ; ☐ PureSperm ; ☐ Percoll ; ☐ Sedimentation
Original : Count : 82 $\times 10^6$ /ml ; Motility : 63 % , Grade I 25 , II 45 , III 30 ; WBC : —
P washing : Count : 40 $\times 10^6$ /ml ; Motility : 99 % , Grade I 0 , II 5 , III 95 ; WBC : —
Comment : —

Oocyte grade	Preincubation (hrs)	Insemination time (sperm Count) (ICSI)	D1 5/1	D2 5/2	D3 5/3	D4 5/4	D5 5/5
1. ++	6 hrs	0.1 x 10 ⁶ /ml	+	2x(II)	8x(II)	12x(II)	Mom/a
2. ++-++			+	2x(II)	8x(II)	Mom/a	BE.4.1B
3. ++-++			+	3x(II)	6x(II)	10x(II)	12x(II)
4. ++-++			+	4x(II)	6x(II)	12x(II)	Mom/a
5. ++-++			+	4x(II)	6x(II)	8x(II)	8x(II)
6. ++-++			+	2x(II)	4x(II)	6x(II)	6x(II)
7. ++-++			+	2x(II)	6x(II)	10x(II)	F
8. ++-++			+	3x(II)	4x(II)	2x(II)	6x(II)
9. ++-++			+	2x(II)	4x(II)	6x(II)	F
10. ++-++	6 hrs	0.1 x 10 ⁶ /ml	+	2x(II)	6x(II)	F	F
1. ++-++	6 hrs	0.1 x 10 ⁶ /ml	+	2x(II)	4x(II)		
2. ++-++			+	2x(II)	4x(II)		
3. ++-++			+	3x(II)	4x(II)		
4. ++-++			+	4x(II)	4x(II)		
5. ++-++			+	4x(II)	4x(II)		
6. ++-++			?	+	2x(II)		
7. ++-++			?	RI	+	2x(II)	
8. ++-++			?	—	—		
9. ++			—	—	—		
10. ++	6 hrs	0.1 x 10 ⁶ /ml	—	RI	—	—	
21. ++-++	6 hrs	0.1 x 10 ⁶ /ml	—	—	—		
22. ++			—	—	—		
23. ++			—	—	—		
24. ++			—	—	—		
25. ++	6 hrs	0.1 x 10 ⁶ /ml	—	—	—		
26. ++			—	—	—		
27. ++			—	—	—		
28. ++			—	—	—		

- 取卵數: 25
- 植入囊胚期胚胎

Oocyte



精蟲形態分析 (Sperm Morphology)

(採用 Kruger's Strict Criteria)

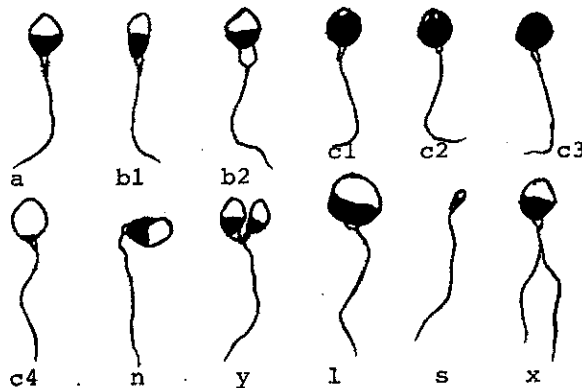
Sperm

正常： a. 正常的精蟲之頭部呈橢圓形，外膜平滑，有清楚的頂體，而頂體佔精蟲頭部之 40%至 70%，並且無頸部、中段或尾部之缺陷。細胞質內之小滴不可超過一半。正常精蟲之頭部長度約 5 至 6um，而直徑約為 2.5 至 3.5um，頸部及尾部正常。

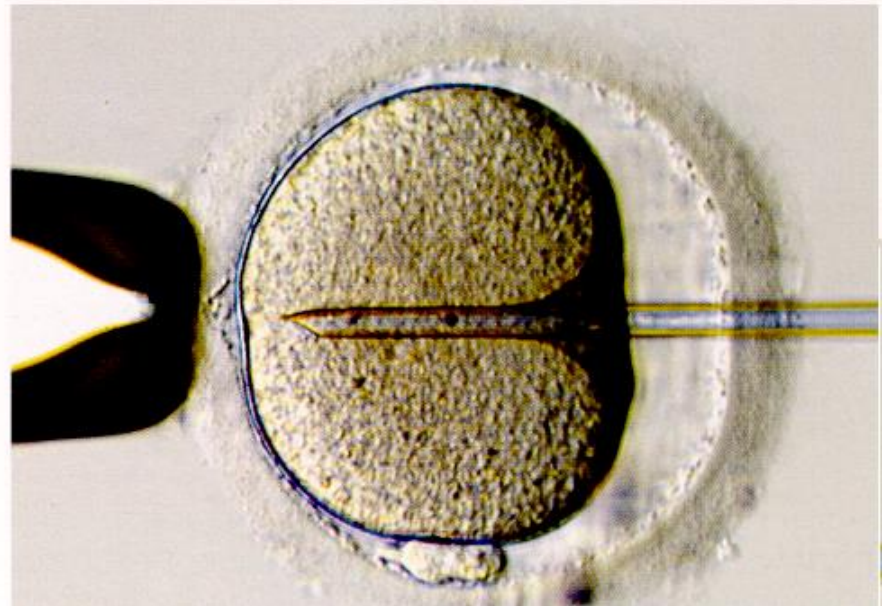
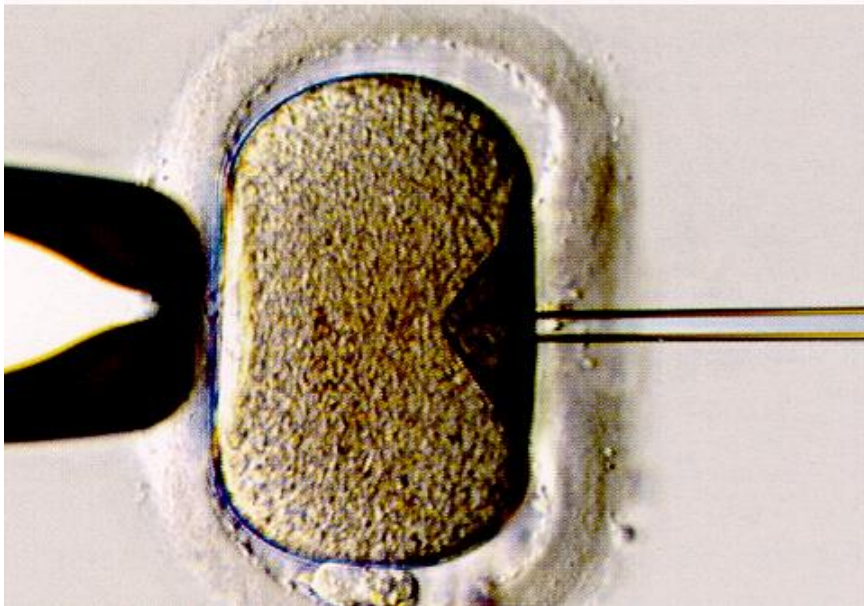
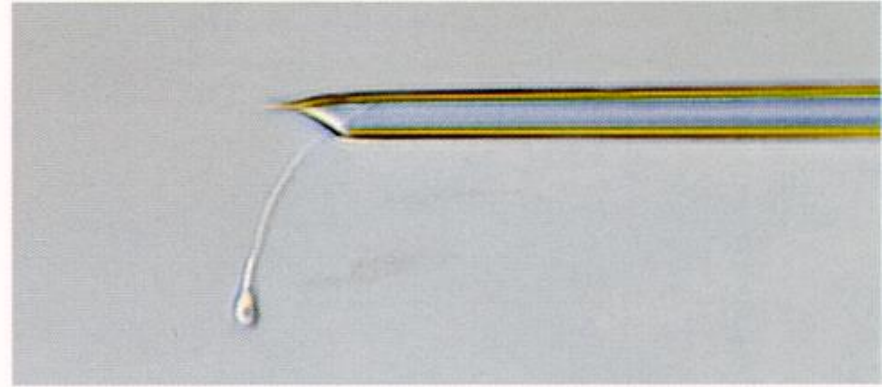
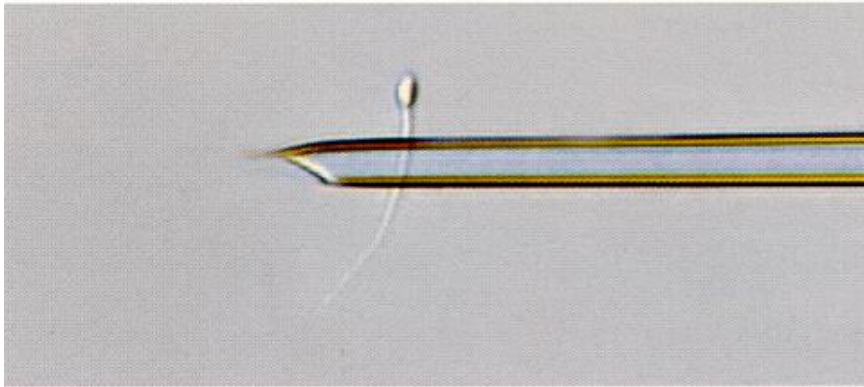
異常： b1. 輕微的變形精蟲頭部：其頭部直徑為 2.0 至 2.5um，頭部之形狀輕微異常，呈較細長的橢圓形，但其頂體仍為正常。
b2. 頸部輕微異常：其頸部有雜質環繞，或頸部增厚而頸部正常。
c. 嚴重的變形精蟲頭部：
c1. 頂體小於精蟲頭部之 30%。
c2. 頂體小於精蟲頭部之 30%，頂體分成數部分。
c3. 不具頂體。
c4. 頂體大於精蟲頭部之 70%
n. 頸部嚴重異常：頸部彎曲或者中段大於 30%。
l. 大頭。 s. 小頭。
y. 雙頭。 x. 雙尾。
o. 其它。



↓ 下圖為各種精蟲形態。



IntraCyttoplasmic Sperm Injection



2pronuclei
4cell

2cell
8cell



Grade 2 embryos

Less than 10% fragmentation *or*
Unequal-sized blastomeres



Grade 3 embryos

10% to 50% fragmentation *with/without*
Unequal-sized blastomeres



Grade 4 embryos

More than 50% fragmentation *with/without*
Unequal-sized blastomeres

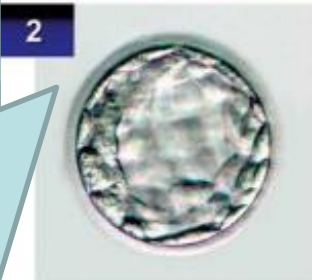
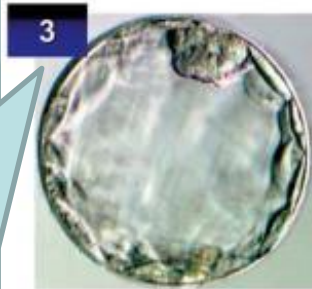


Morula and Blastocyst



system used to evaluate blastocyst expansion, inner cell mass characteristics, and trophectoderm morphology.

Expansion



Inner Cell Mass

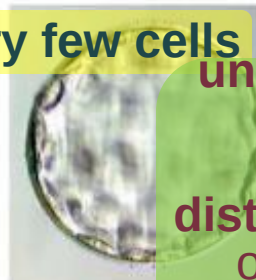
Tightly compacted cells



larger, loosely grouped cells



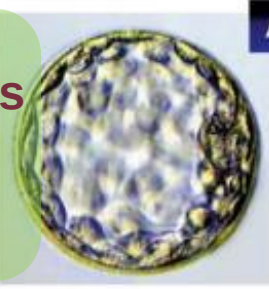
Very few cells



degenerative

Trophectoderm

many healthy cells forming a cohesive epithelium



few but healthy cells, large in size, forming a loose epithelium



unhealthy, very large, or unevenly distributed cells, or few cells squeezed to the side



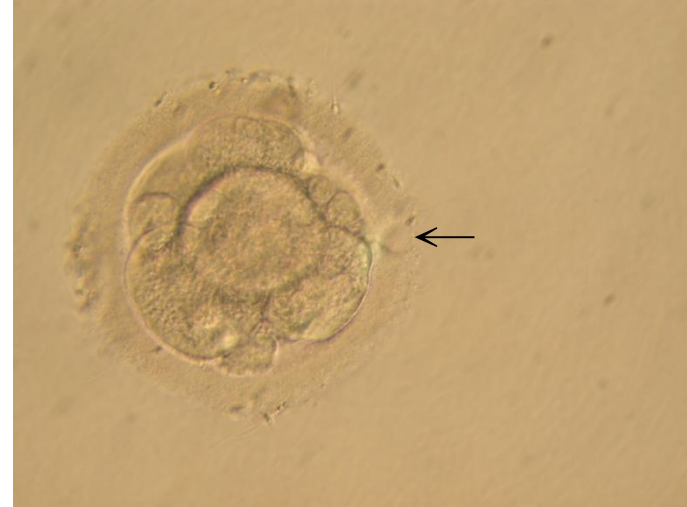
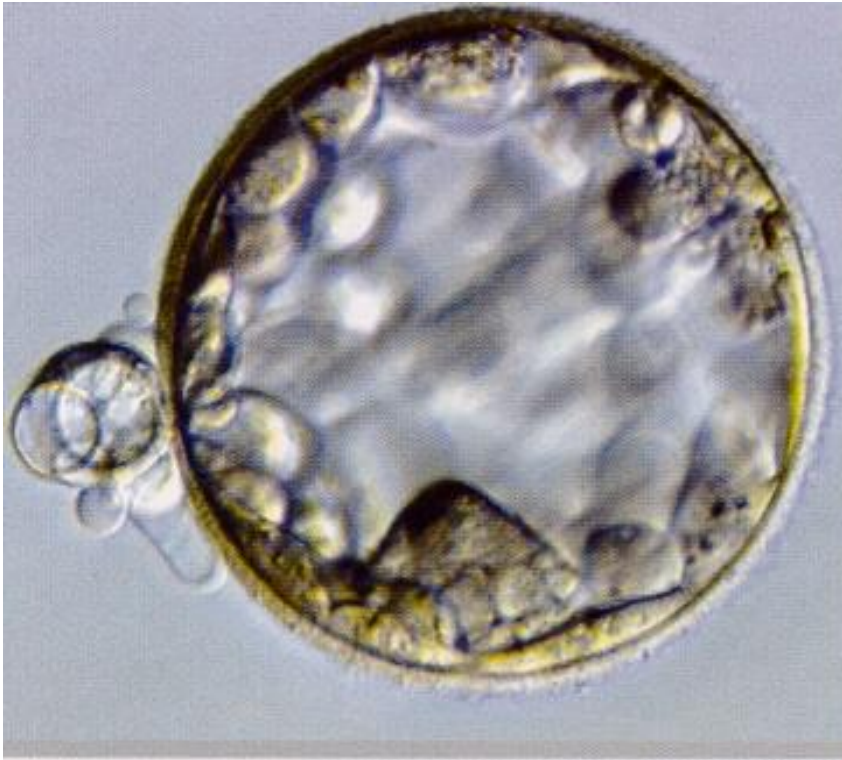
degenerative

3 (a full blastocyst): blastocoel completely fills the embryo with overall size fully enlarged and a very thin zona pellucida with slight expansion in overall size and some thinning of the zona pellucida. NO overall size increase.

4: a hatching blast 5: a fully hatched blast

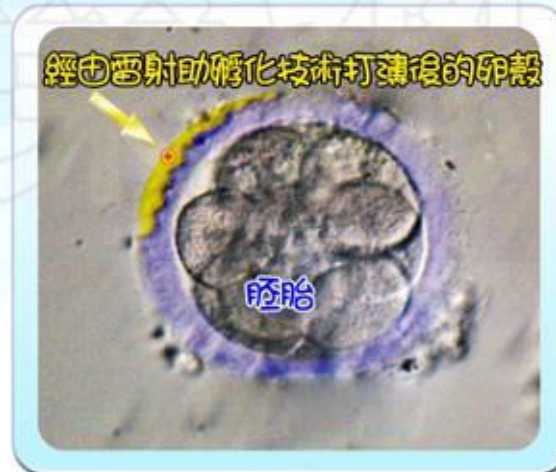
6: a hatching or hatched blastocyst resulting from assisted hatching or biopsy

Hatching and Assisted Hatching



蛋殼太硬怎麼辦？

胚胎要著床之前必須先破殼而出完成孵化，胚胎有時候會因為透明帶（卵殼）太硬、太厚，無法分泌溶解酵素或其他的障礙，導致胚胎無法破殼、孵化及著床。



本院婦產部生殖醫學中心配有

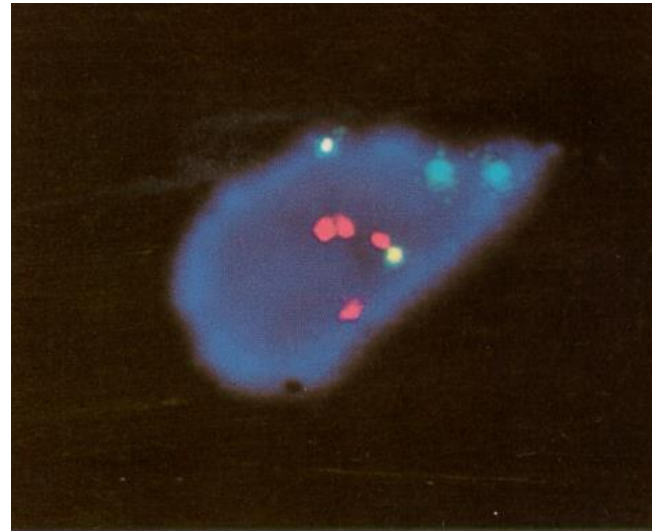
最新式

雷射助孵化系統

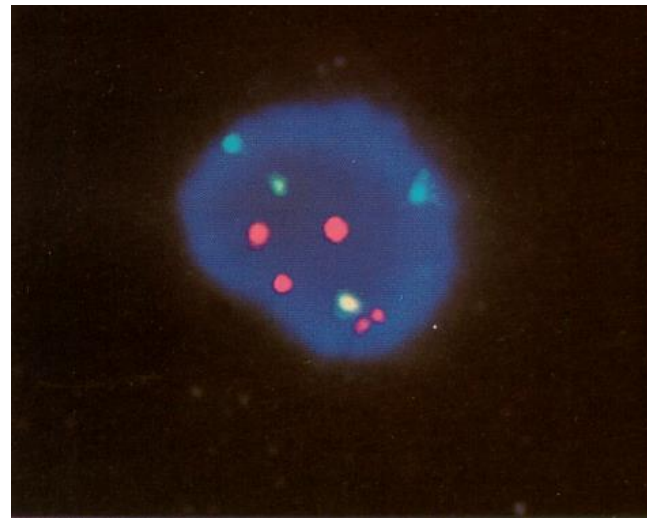
PGD and FISH

X: yellow Y: blue-green

18: green 13/21: red



Normal
XY

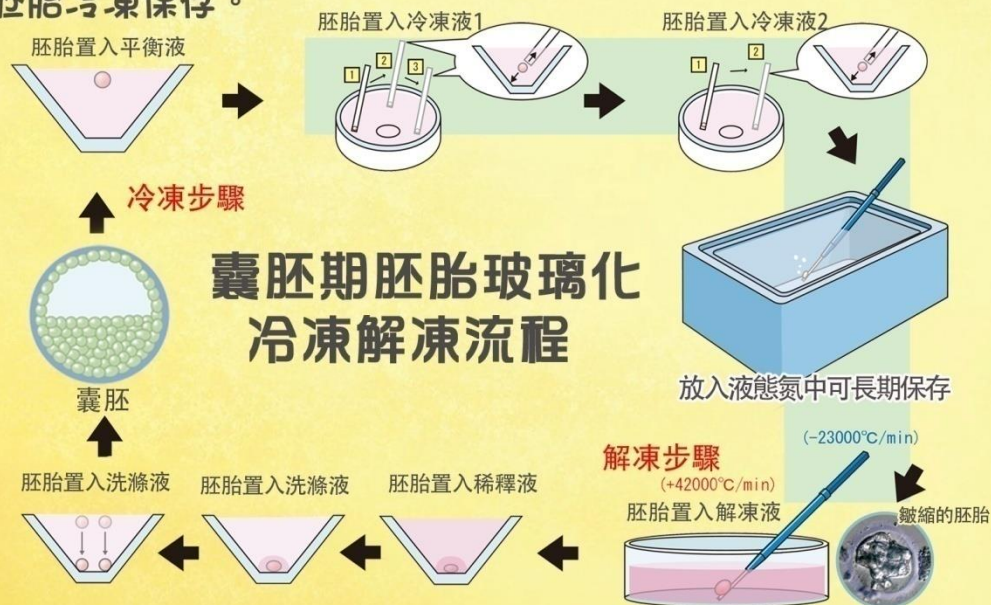


Trisomy
13 or 21

儲存寶貝生命的最新方法

囊胚期胚胎玻璃化冷凍 (Vitrification)

執行試管嬰兒療程中，目前人工生殖法規定最多植入胚胎數為4顆，剩餘未植入的優質胚胎，可利用冷凍方法將胚胎冷凍保存。



利用高濃度的冷凍保護劑將細胞內水份脫水，瞬間變成高黏稠固態的非結晶玻璃狀物質，使細胞內冰晶來不及形成就被冰凍起來，降低冰晶對胚胎的傷害，因此被稱為玻璃化冷凍。

由於此技術的發明，大大提升了冷凍胚胎的懷孕率，高雄榮總婦產部生殖醫學中心平均冷凍胚胎懷孕率為**45%**，若您進入試管嬰兒療程植入後仍有多餘胚胎，可利用胚胎冷凍方式儲存寶貝的生命呦。

在超音波導引下,確認胚胎最佳植入位置



台灣的國民健康署資料:2015年植入新鮮胚胎共 10,804 週期及植入冷凍胚胎共 8,604 週期

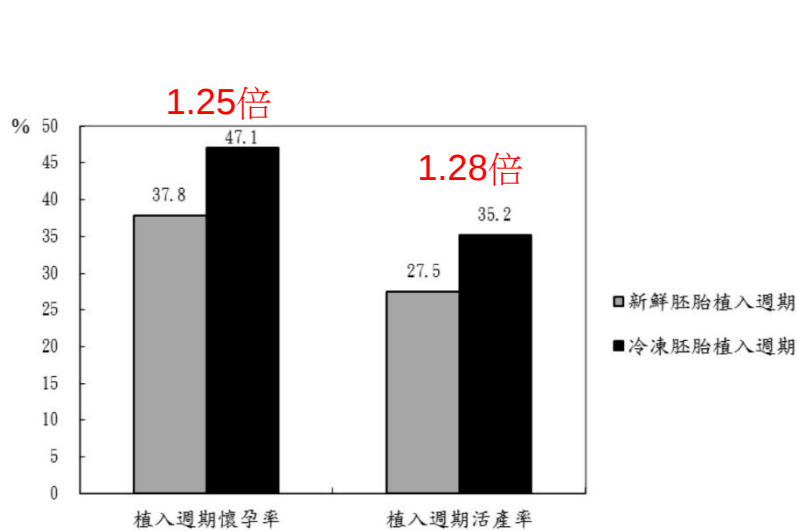


圖 14 104 年配偶間人工生殖植入新鮮胚胎及冷凍胚胎之成功率比較

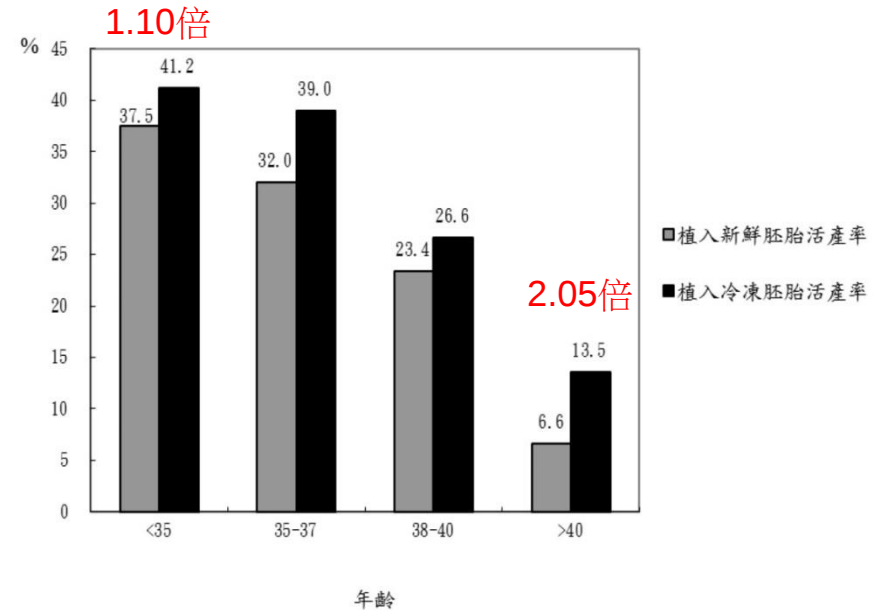
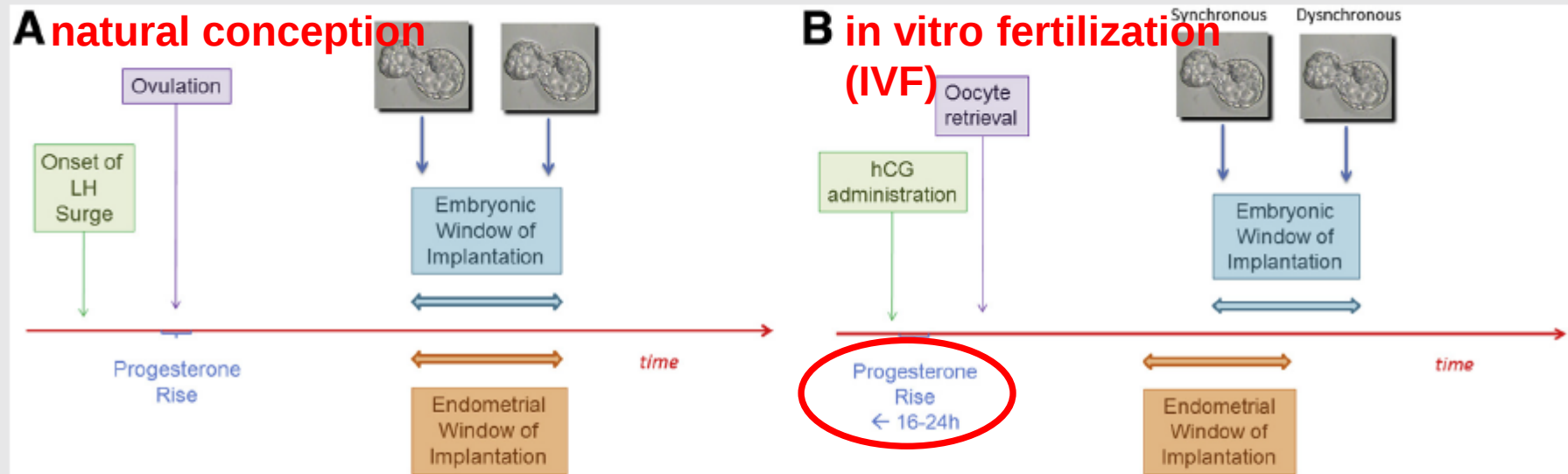


圖 16 104 年配偶間人工生殖植入新鮮胚胎及冷凍胚胎之受術妻年齡別活產率

懷孕率及活產率：凍胚植入 > 鮮胚植入 ($P < 0.0001$)，女性年齡越高此差距越大！

FIGURE 1

Embryo and endometrial synchrony involves both the endometrium, whose window is determined by the progesterone stimulus, and the embryo, whose window is relative to blastulation. (A) During natural conception, a rise in progesterone follows the luteinizing hormone surge and leads to the opening of the endometrial window of receptivity, which overlaps with the window of embryonic blastulation and implantation. (B) In in vitro fertilization, natural coordination can be lost. The rise in progesterone after the ovulation trigger is faster and more robust, and the progesterone stimulus shifts the endometrial window of receptivity by 16 to 24 hours. Additionally, blastulation may be delayed, particularly in older, low responders. These two factors, either alone or together, result in a physiologic dyssynchrony that cannot be predicted before the cycle start and may not necessarily be reproduced from cycle to cycle.

Franasiak. Endometrial and embryo dyssynchrony. Fertil Steril 2016.

Fertil Steril 2016;105:861 – 6.

- A. Natural conception:
 - # LH surge → ovulation → oocyte exposed to spermatozoa → embryonic window of implantation (WOI, blastulation)
 - # meaningful P shortly after LH surge↑ → secretory transformation → endometrial window of implantation (WOI)
- B. IVF (lost of natural coordination = embryonic-endometrial dyssynchrony):
 - 1. P ↑ faster (16~24 hr)
 - 2. blastulation may be delayed (older, low responders)

Endometrium preparation for FET

