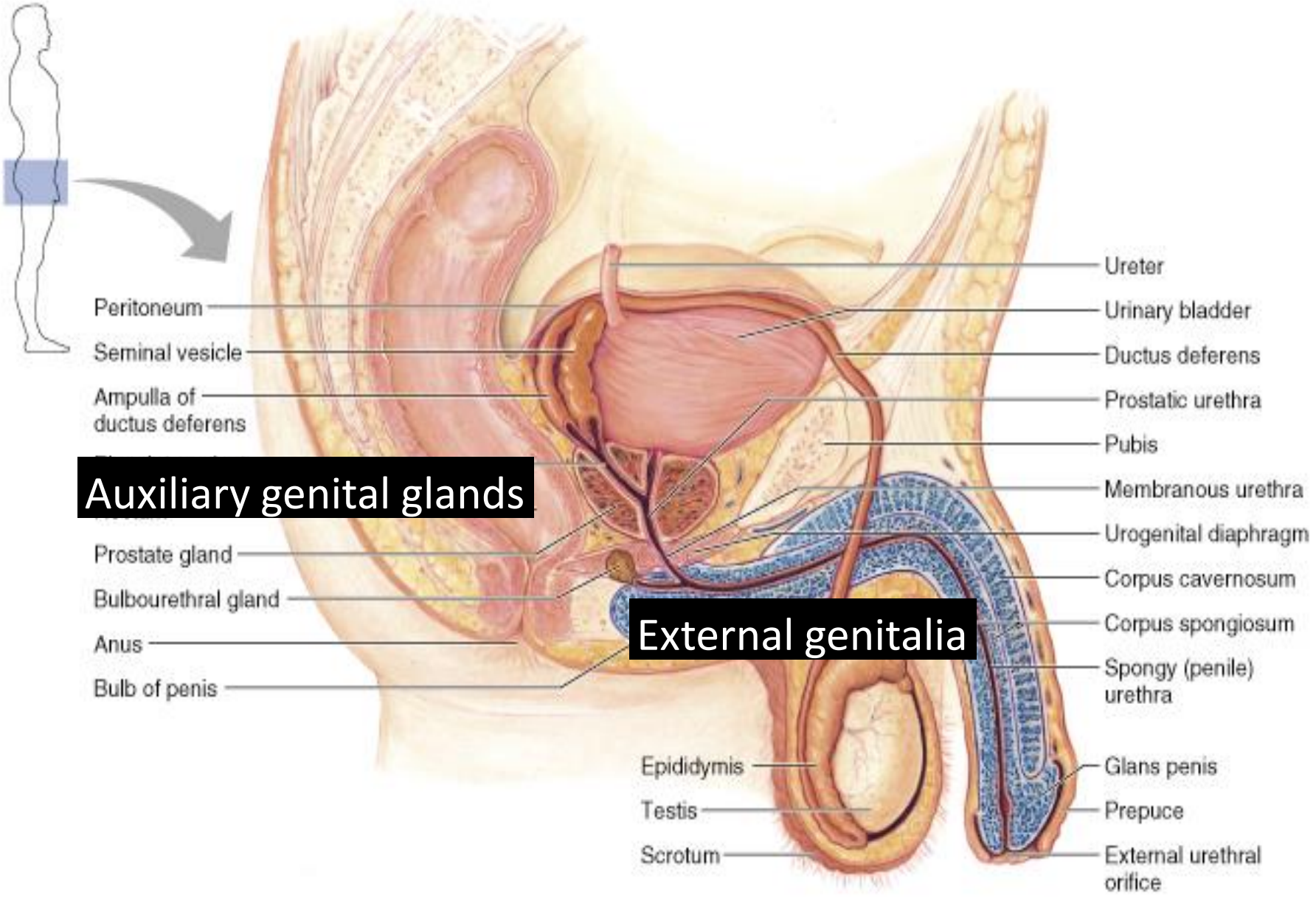
Male reproductive anatomy, physiology and andrology

- 以胚胎學來看, 睪丸於第七週開始形成
- 第八週時,睪丸製造兩種荷爾蒙: (1) Testosterone (T) (2) Mullerian-inhibition protein (MIP)
- T 從 Leydig cell分泌, 促使同側Wolffian duct 分化成epididymis and vas deferens 並開始成形
- MIP 從Sertoli cell, 抑制Mullerian duct使其退化成 testicular appendix.
- 第八到第十六週形成外生殖器. 由testosterone 經5a reducatase 成 dihydrotestosteron (DHT), 誘發外生殖器產生
- 正常男性一天製造約5-7g testosterone.
- 在血液中與 albumin (38%), SHBG (60%)結合. 2% free form bioactive.
- 代謝物 DHT 與 estradiol

Male reproductive system



Auxiliary genital glands

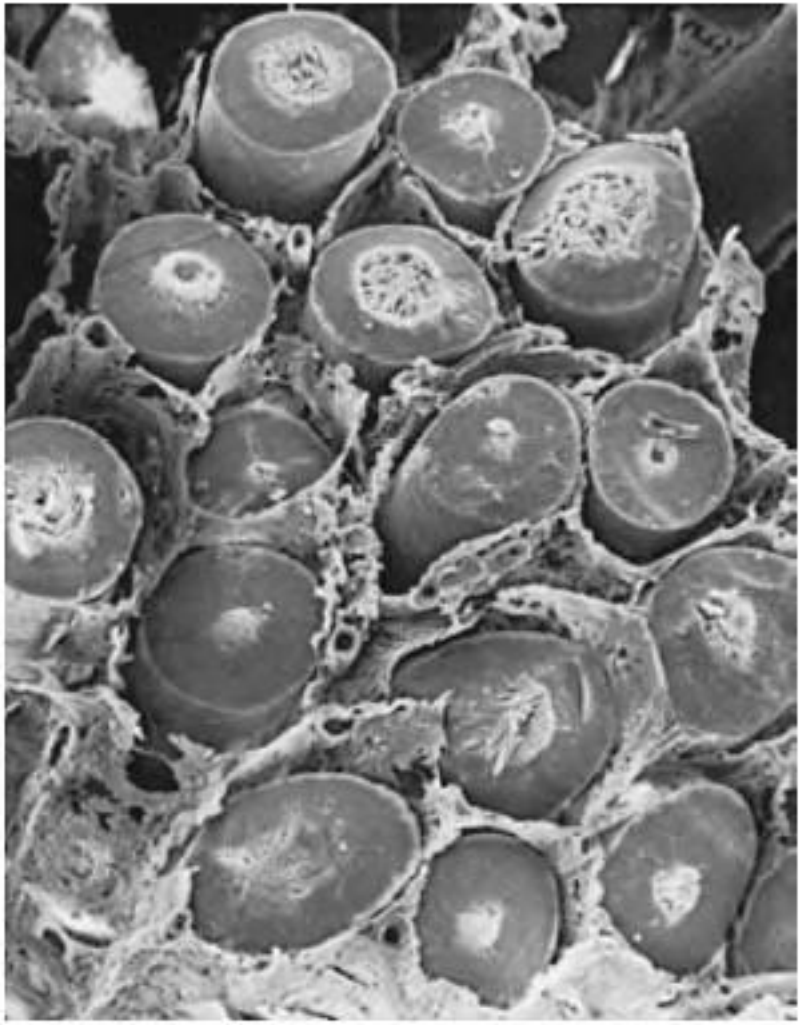
- Prostate
  - thin, milky and alkaline fluid to enhance the motility.
- Seminal vesicles
  - fructose: energy for sperm
  - prostaglandins: mobility and viability of the sperm; and
  - proteins that cause slight coagulation reactions in the semen after ejaculation.
- bulbourethral glands
  - neutralizes the acidity of the urine residue in the urethra, helps to neutralize the acidity of the vagina, and provides some lubrication for the tip of the penis during intercourse.

External genitalia

- Penis
  - copulation and urinary excretion
- Vas deferens (ductus deferens)
  - route for sperm transportation
- Epididymis (head, body and tail)
  - spermatozoa maturation
- Testes
  - spermatozoa production occurs within the epithelial lining of smeniniferous tubules

Seminiferous tubules

- Approx. 90-120m
- have a basement membrane consisting of elastic and connective tissue
- seminiferous cells are either Sertoli cells (supporting cells) or spermatogenic cells.
- Found embedded in interstitum are Leydig cells which produce testosterone



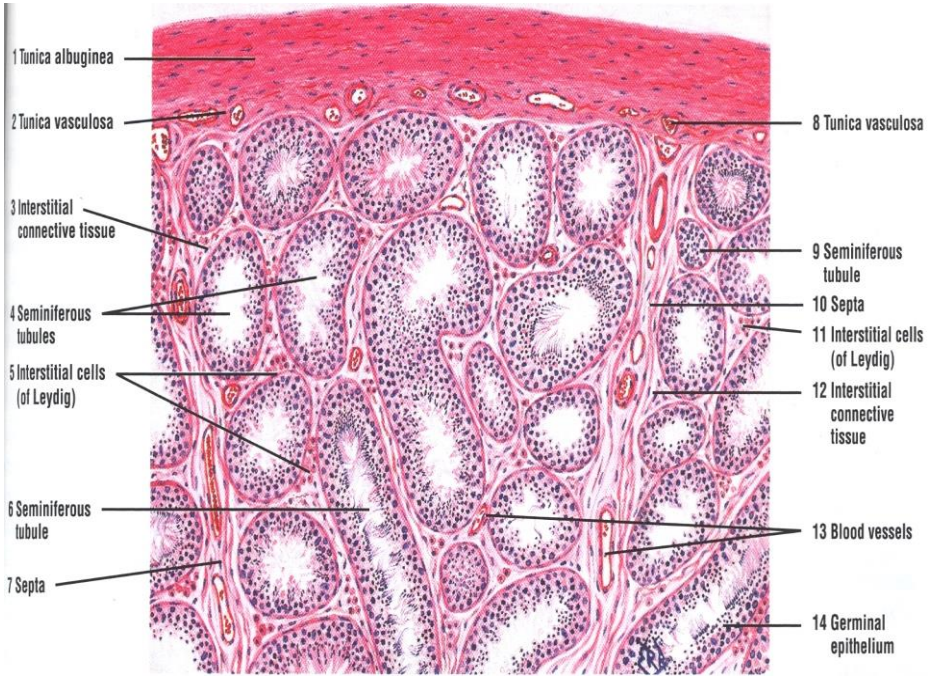
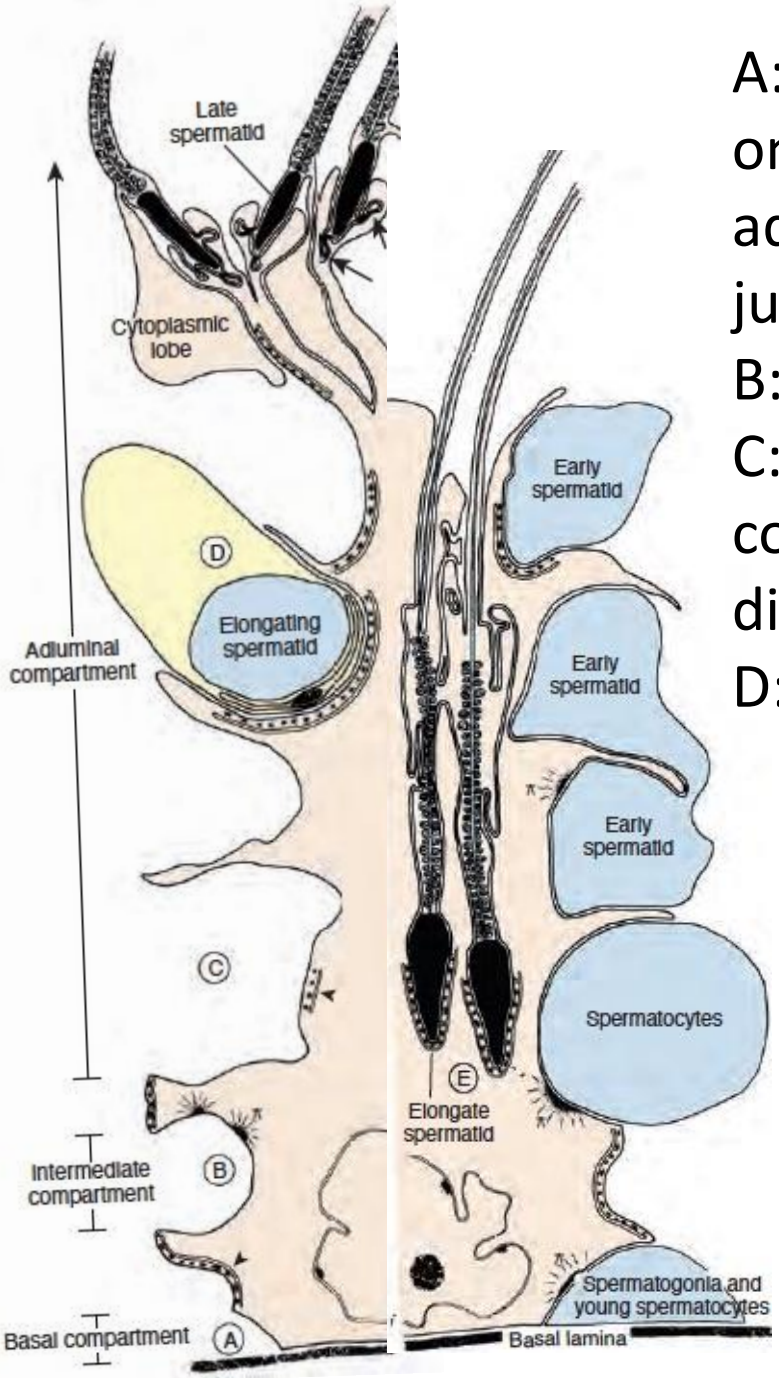


Figure 22-5. **Scanning electron micrograph of the cut surface of the human testis. Note the relationship of interstitial tissue to seminiferous tubules. (From Christensen AK. Leydig cells. In: Greep RO,**

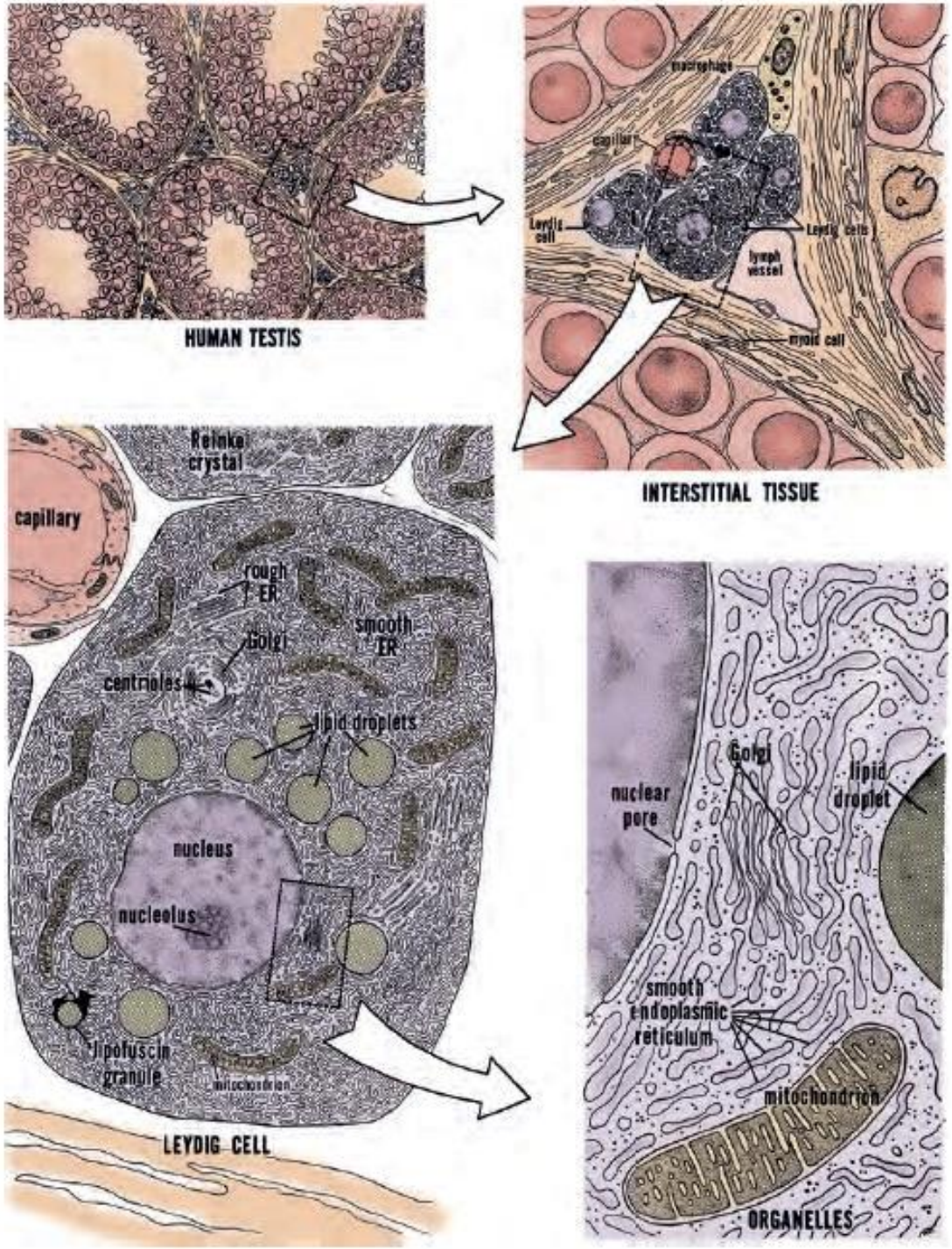


A: spermatogonia and early spermatocytes on basal lamina and enveloped by adjacent Sertoli cells that join to form tight junction (B-T barrier)

B: Sertoli cells form junctional complexes

C: Spermatocytes enter adluminal compartment when sertoli tight junction dissociate.

D: Elongating spermatid


HUMAN TESTIS
macrophage
capillary
Leydig cell
Leydig cells
lymph vessel
myoid cell
INTERSTITIAL TISSUE
Reinke crystal
capillary
rough ER
smooth ER
Golgi
centrioles
lipid droplets
nucleus
nucleolus
lipofuscin granule
mitochondrion
LEYDIG CELL
nuclear pore
Golgi
lipid droplet
smooth endoplasmic reticulum
mitochondrion
ORGANELLES

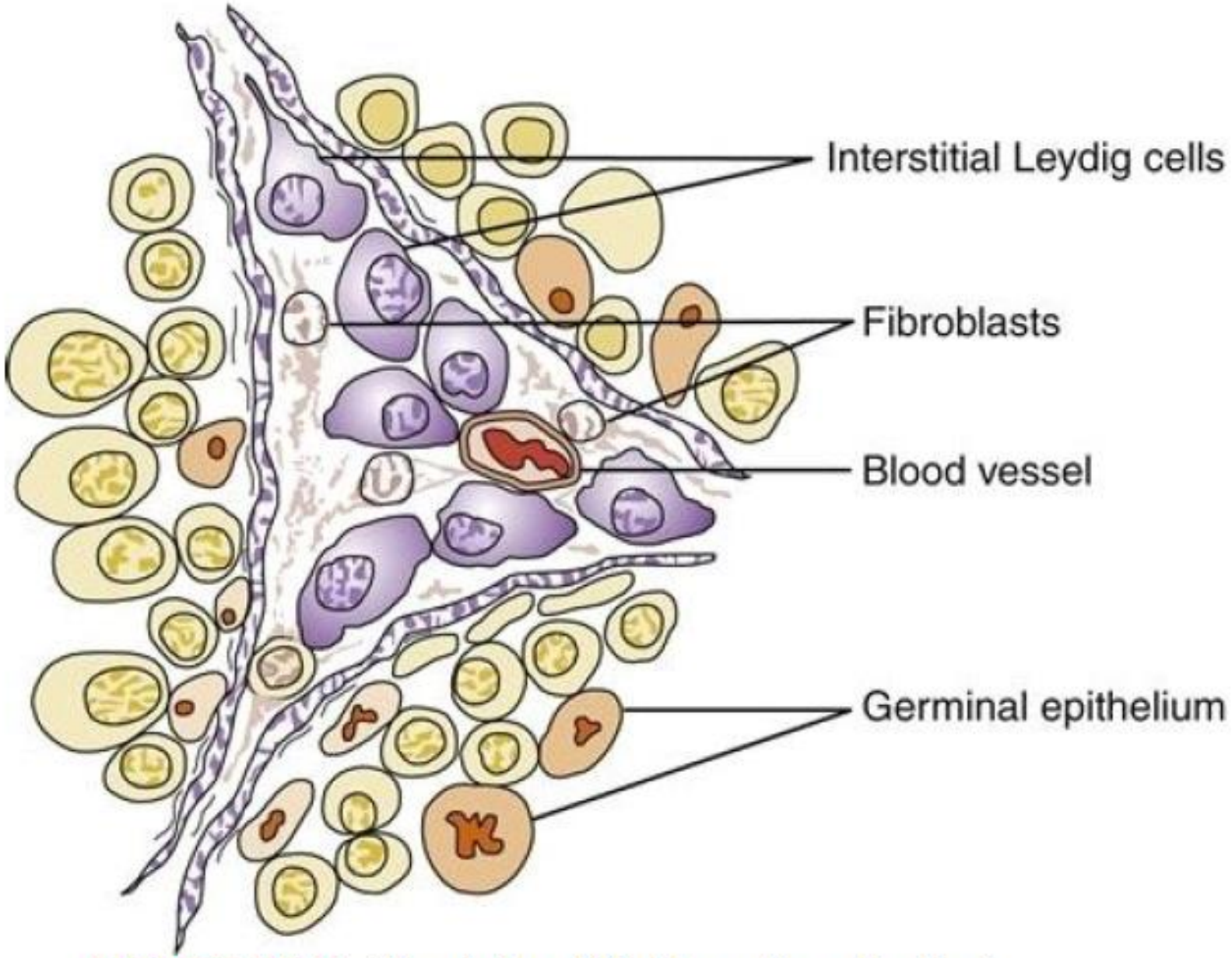
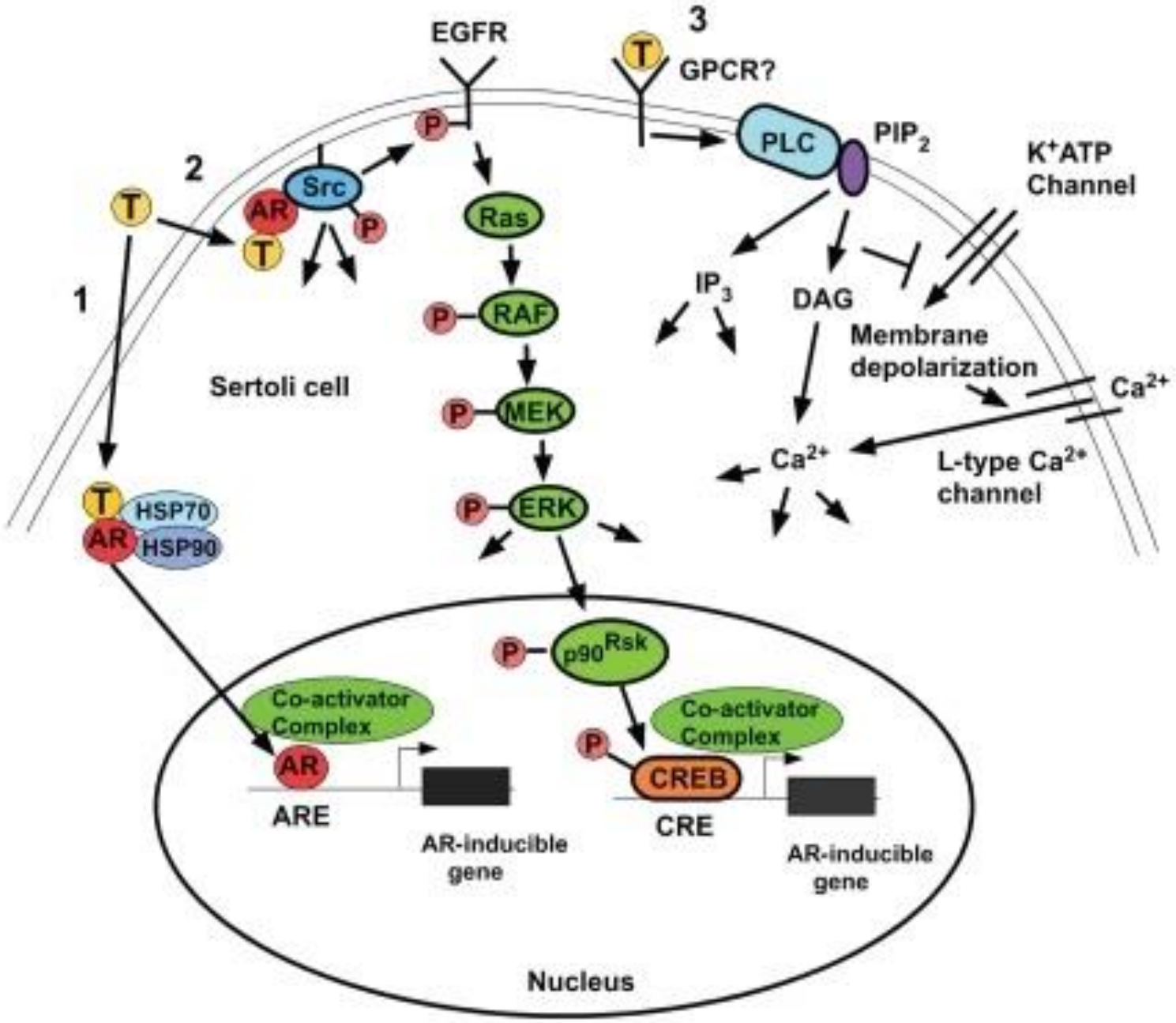


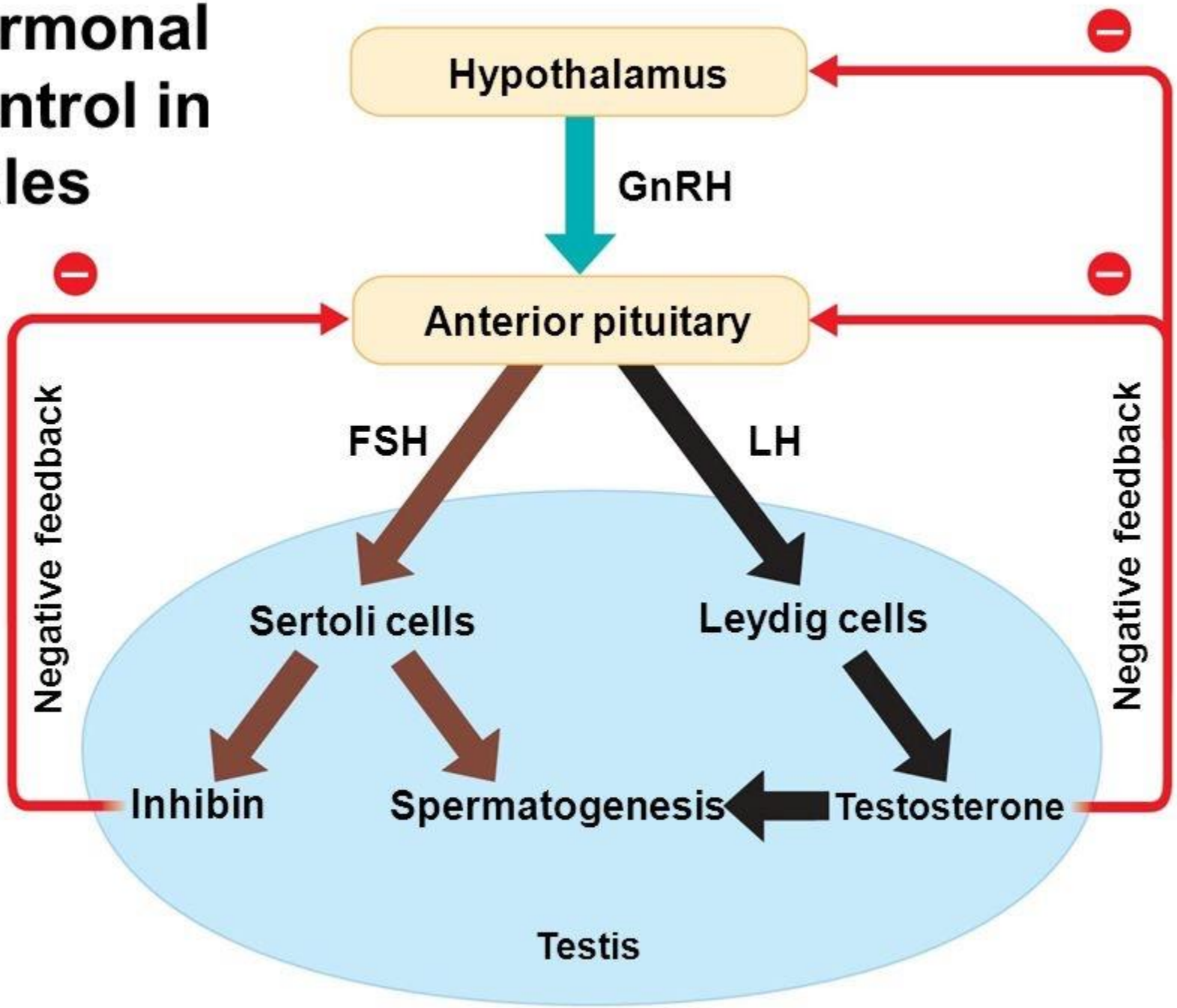
FIGURE 30-7 **The interstitial Leydig cells that secrete testosterone are located in the interstices between the seminiferous tubules.** (From Hall JE, editor:

Testosterone signalling and spermatogenesis regulation

- Absence of testosterone or the androgen receptor, spermatogenesis does not proceed beyond the meiosis stage.
- The major cellular target and translator of testosterone signals to developing germ cells is the Sertoli cell.
- In the Sertoli cell, testosterone signals can be translated directly to changes in gene expression (the classical pathway) or testosterone can activate kinases that may regulate processes required to maintain spermatogenesis (the non-classical pathway).

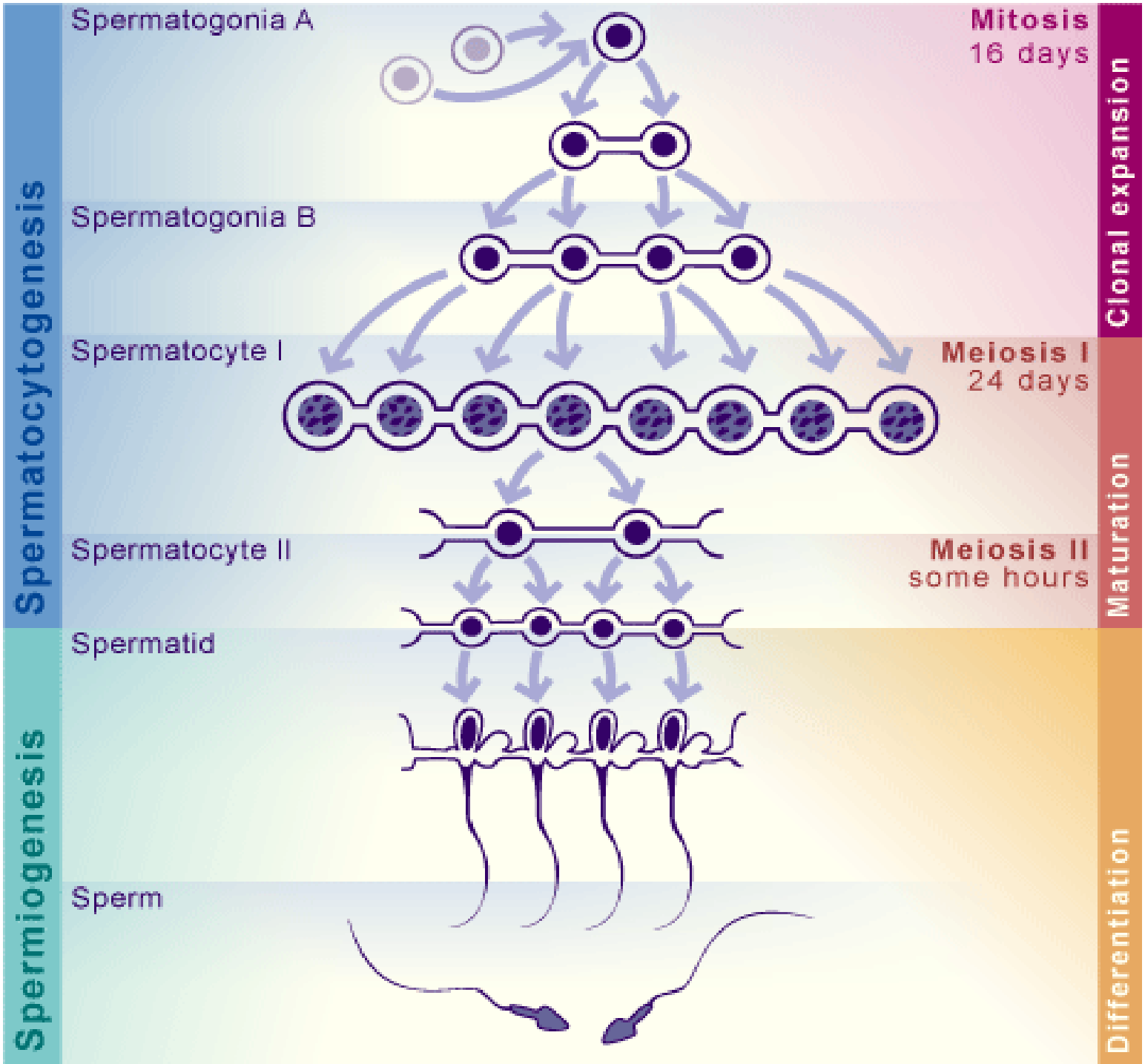

EGFR
3
GPCR?
T
PLC
PIP2
K+ATP
Channel
2
Src
AR
P
T
Ras
1
P
RAF
IP3
DAG
Membrane
depolarization
Ca2+
Sertoli cell
P
MEK
Ca2+
L-type Ca2+
channel
T
HSP70
AR
HSP90
P
ERK
P
p90Rsk
Co-activator
Complex
Co-activator
Complex
AR
P
CREB
ARE
CRE
AR-inducible
gene
AR-inducible
gene
Nucleus

Hormonal Control in Males



Spermatogensis

- in vivo kinetic study revealed duration of spermatogenesis ranges from 42 to 76 days.
  - spermatocytogensis (proliferative phase)
    - spermatogonia self-renewal or
    - differentiation (spermatocytes)
  - meiotic phase
    - reduction division, resulting in haploid spermatids
  - spermiogensis phase
    - mature spermatozoa


Spermatocytogenesis
Spermiogenesis
Spermatogonia A
Spermatogonia B
Spermatocyte I
Spermatocyte II
Spermatid
Sperm
Mitosis
16 days
Meiosis I
24 days
Meiosis II
some hours
Clonal expansion
Maturation
Differentiation

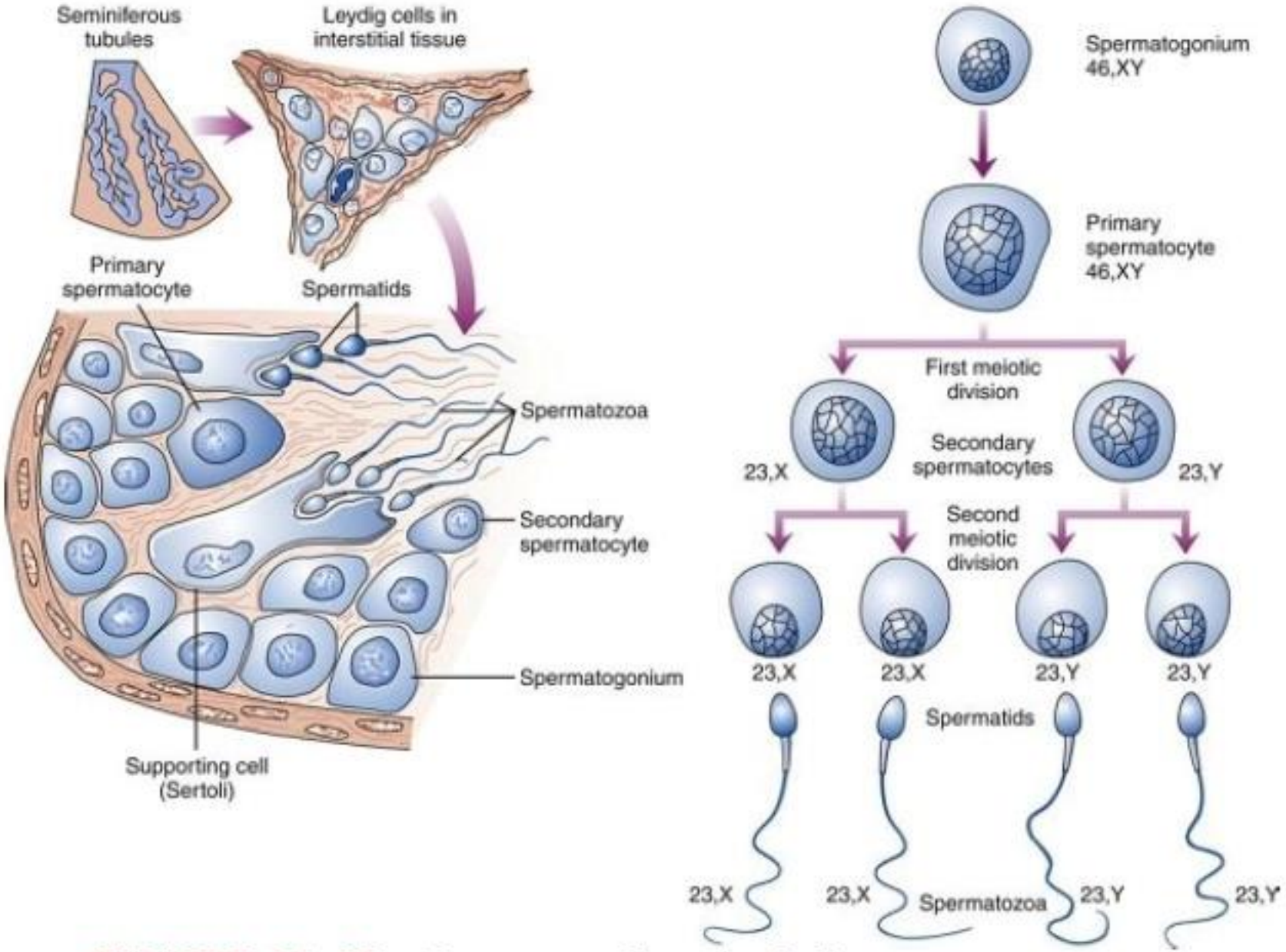
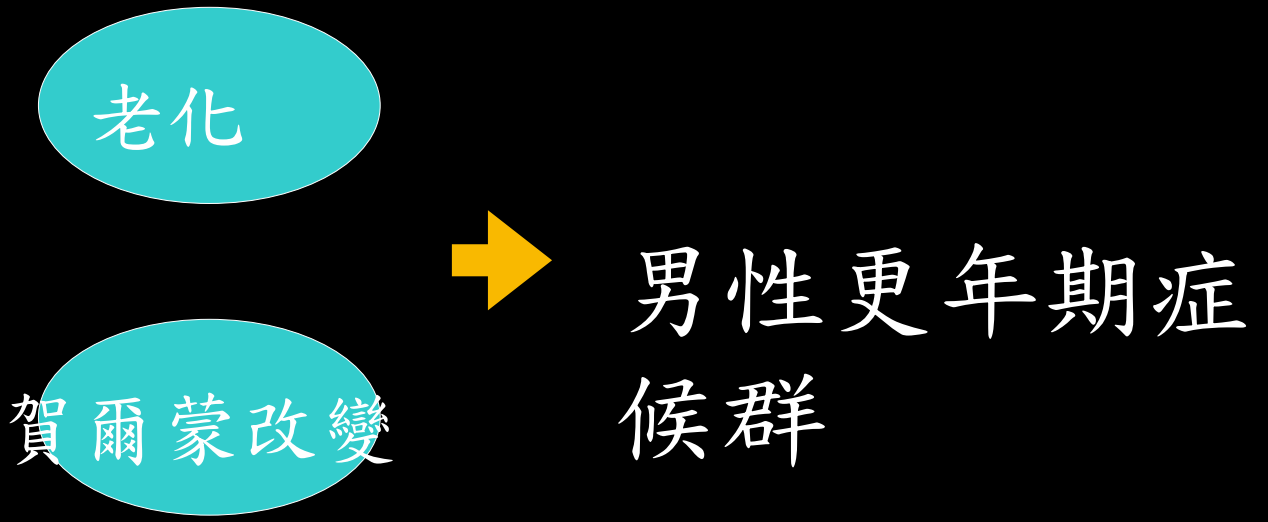
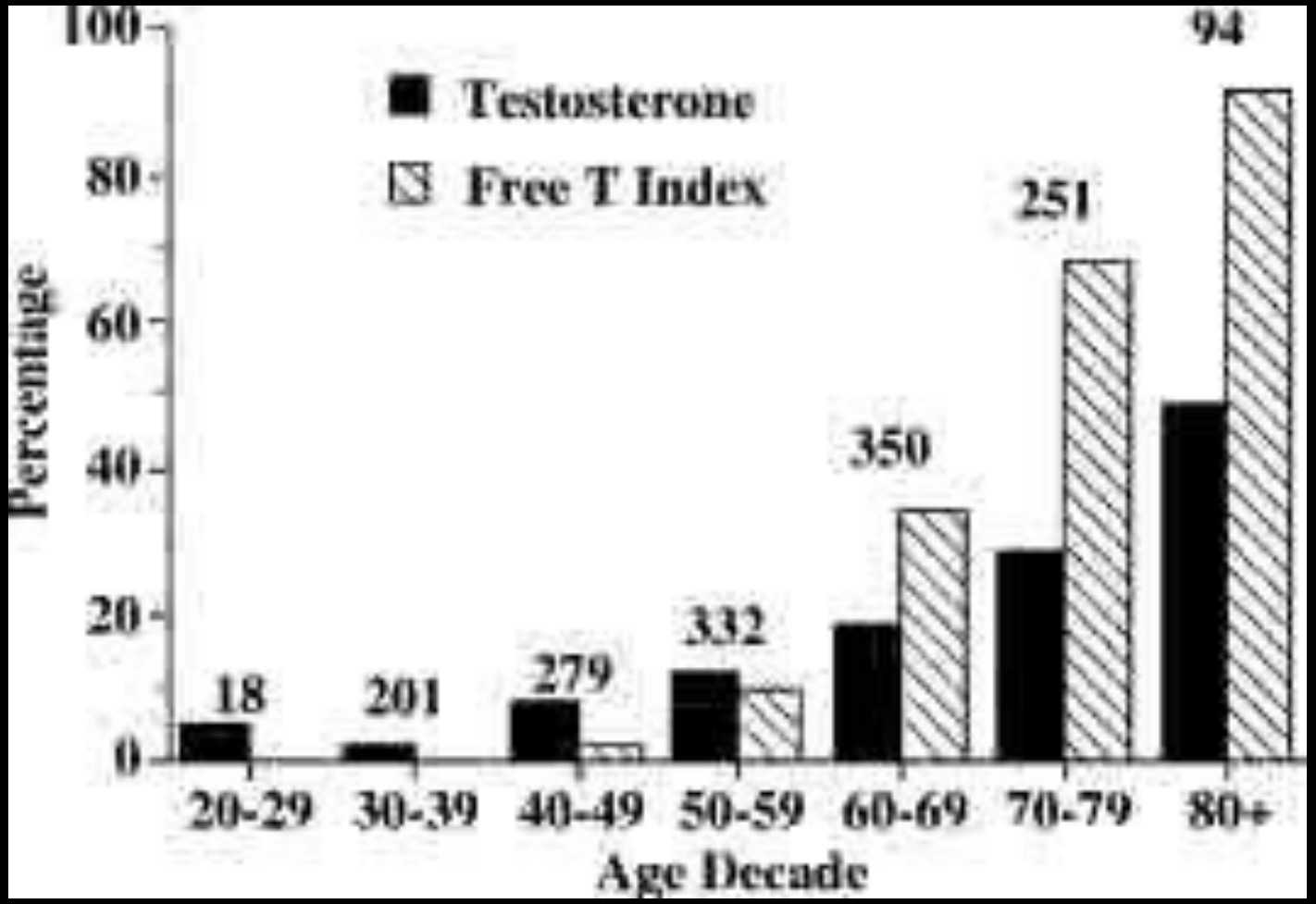


FIGURE 30-15 **Process of meiosis in spermatogenesis.**

真有男性更年期？




100
80
60
40
20
0
Percentage
Testosterone
Free T Index
18
201
279
332
350
251
94
20-29
30-39
40-49
50-59
60-69
70-79
80+
Age Decade

Androgen Deficiency in Aging Male

Late onset hypogonadism

- The prevalence of symptomatic androgen deficiency may be up to 12% in males older than 40 years of age.
- Various interchangeable descriptions have been used in the literature. these include ‘testosterone deficiency’, ‘andropause’ and ‘late onset hypogonadism’ (LOH).
- LOH may be defined as ‘a clinical and biochemical syndrome associated with advancing age and characterized by typical symptoms and a deficiency in serum tesotonerone (T) levels.

Etiology of LOH

- Androgen levels decrease by approximately 1% per year after the age of 40 and the levels of SHBG increase with age, resulting in reduced bioavailable (free) T.
- Low T levels in the aging male can be associated with chronic conditions such as obstructive sleep apnoea, depression, obesity, COPD, DM and renal or liver disease.
- Drugs (eg. opiates, glucocorticoids, and gonadotropin- releasing hormone agonists such as finasteride, oestrogen, spironolactone and ketoconazole) will reduce T secretion and/or its effect.

Diagonsis and presentation

- Diagnosis of loh requires two elements: the presence of at least one clinical symptom and biochemical confirmation fo low total T levels.

男性更年期症候群的臨床表徵

新陳代謝的變化：骨質疏鬆、肥胖、糖尿病

自主神經的變化：全身發燙、臉潮紅、流冷汗、心跳加快、腸胃不適、便秘等等…。

精神神經的變化：記憶力減退、容易疲勞、缺乏衝勁、不能集中精神、焦慮、抑鬱、失眠等等…..　。

下泌尿症狀：頻尿、小便困難

性功能衰退：性慾減低、勃起障礙、射精量減少沒有快感…。

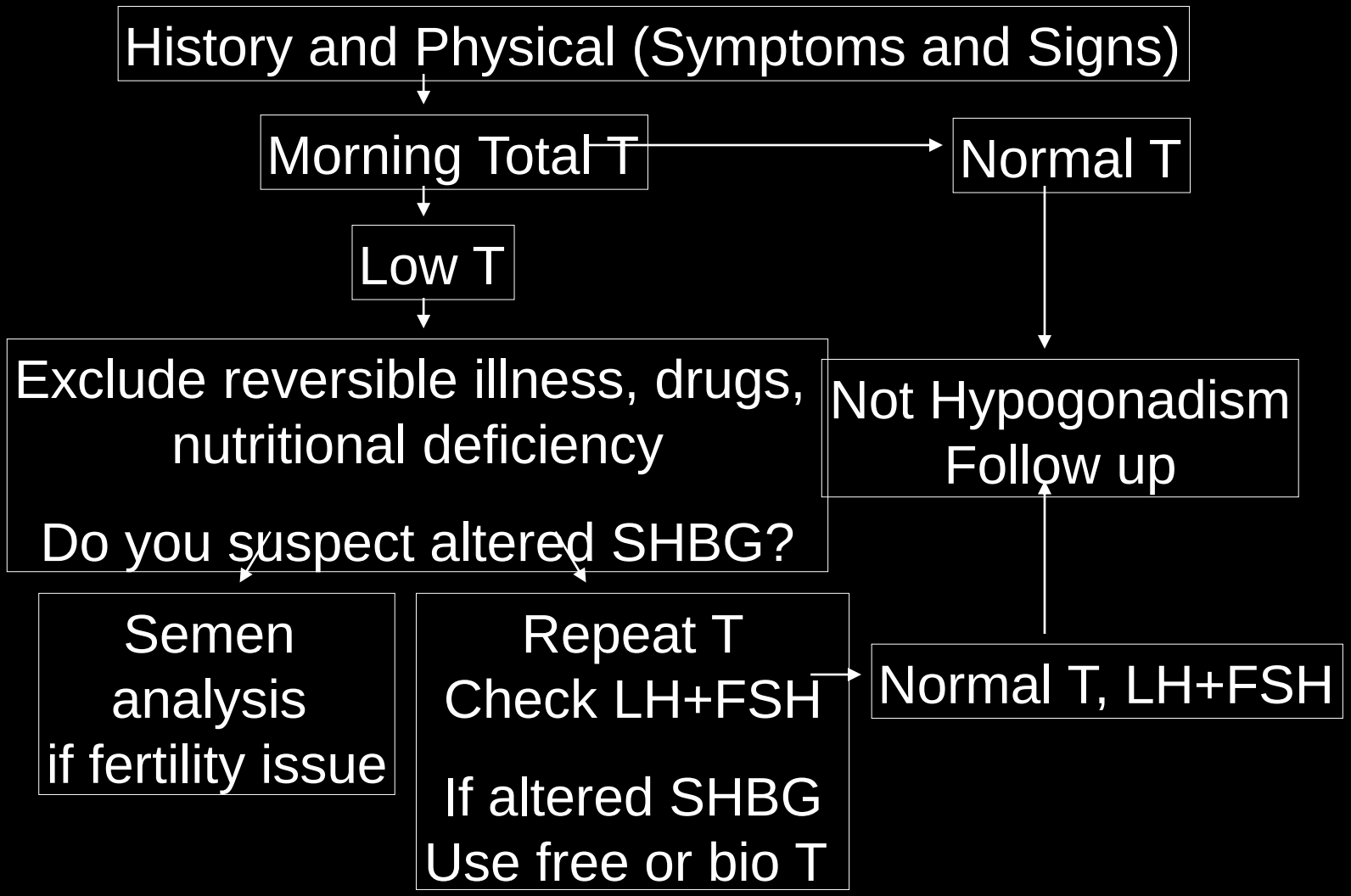
如何知道自己有男性更年期症狀?

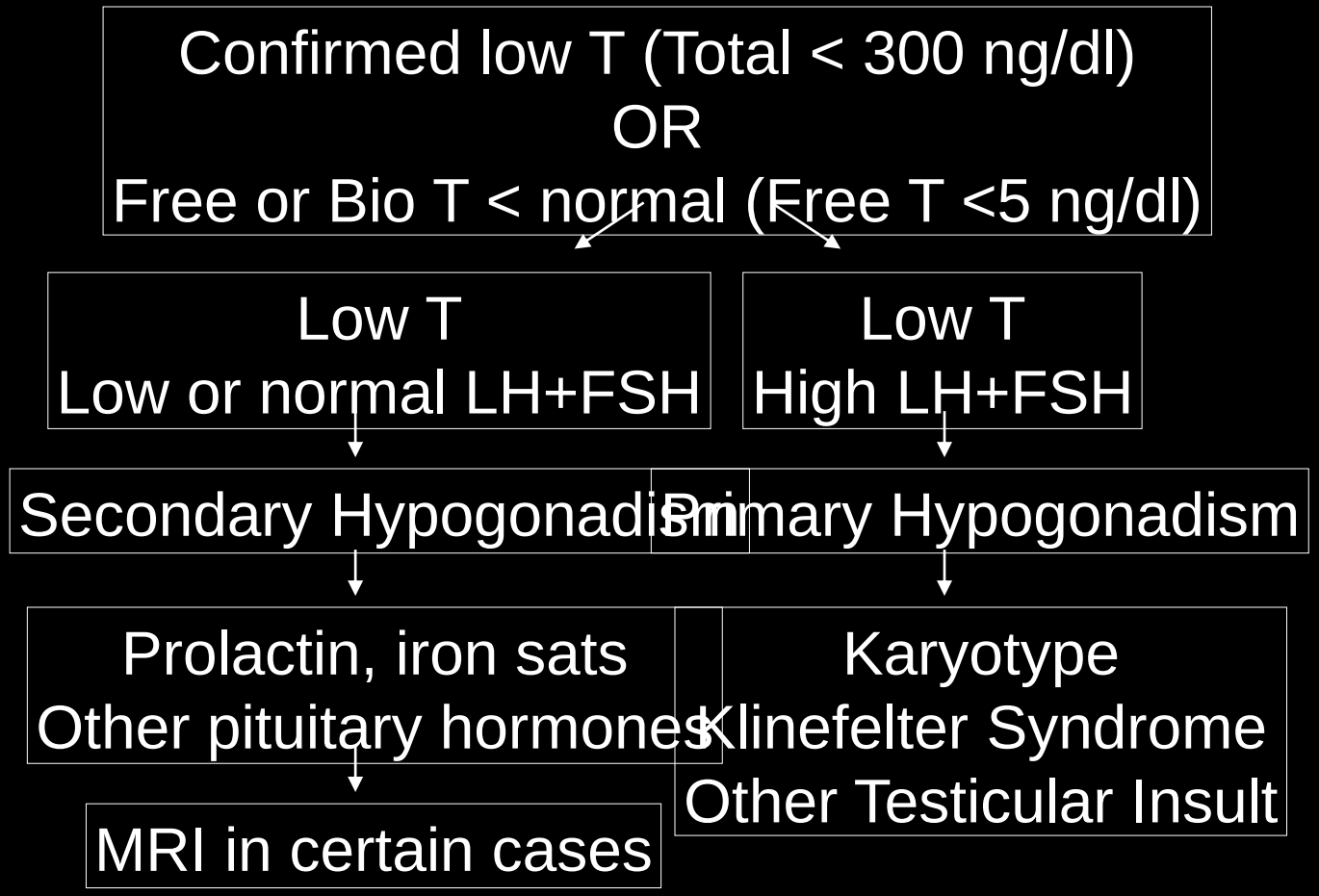
聖路易大學老化男人睪固酮低下問卷可用於患者的初步篩選

The Saint Louis University Androgen Deficiency in Aging Males (ADAM) questionnaire

第1或7題回答「是」，或是其他八題有任三題回答「是」者，就需要進一步確認是否為睪固酮低下症患者

1. 您是否有性慾(性衝動)降低的現象？
2. 您是否覺得比較沒有元氣(活力)？
3. 您是否有體力變差或耐受力下降的現象？
4. 您的身高是否有變矮？
5. 您是否覺得生活變得比較沒樂趣？
6. 您是否覺得悲傷或沮喪？
7. 您的勃起功能是否較不堅挺？
8. 您是否覺得運動能力變差？
9. 您是否在晚餐後會打瞌睡？
10. 您是否有工作表現不佳的現象？


History and Physical (Symptoms and Signs)
Morning Total T
Normal T
Low T
Exclude reversible illness, drugs, nutritional deficiency
Do you suspect altered SHBG?
Not Hypogonadism Follow up
Semen analysis if fertility issue
Repeat T Check LH+FSH
If altered SHBG Use free or bio T
Normal T, LH+FSH


Confirmed low T (Total < 300 ng/dl)
OR
Free or Bio T < normal (Free T <5 ng/dl)
Low T
Low or normal LH+FSH
Low T
High LH+FSH
Secondary Hypogonadism
Primary Hypogonadism
Prolactin, iron sats
Other pituitary hormones
MRI in certain cases
Karyotype
Klinefelter Syndrome
Other Testicular Insult

T therapy

- Improve/maintain secondary sexual characteristics
- Improve libido and erections
- Increase energy and well-being
- Improve muscle mass and strength
- Improve bone mineral density

Contraindications to T Therapy

- Uncontrolled Prostate cancer
- Lump/hardness on prostate exam by DRE
- PSA >3 ng/ml that has not been evaluated for prostate cancer
- Severe untreated BPH (AUA/IPSS >19)
- Erythrocytosis (hematocrit >50%)
- Hyperviscosity
- Untreated obstructive sleep apnea
- Severe heart failure (class III or IV)

Testosterone Options

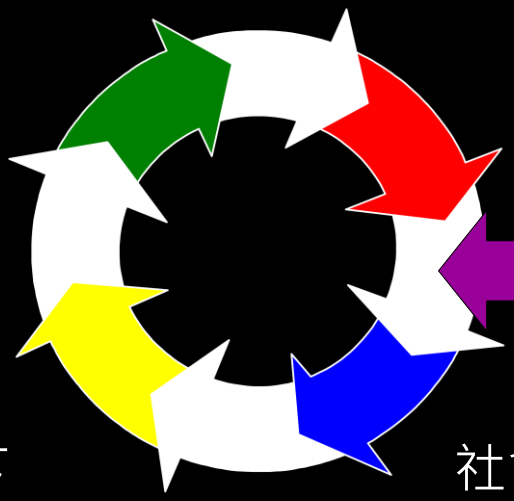
New: Fortesta (2 % gel)

Safety monitoring

- Baseline
  - Testosterone level
  - DRE
  - PSA
  - Hematocrit
- Follow-up ~3 months then annually
  - Assess improvement/side effects
  - Testosterone level
  - DRE
  - PSA
    - age- and race-appropriate interval
  - Hematocrit
- If osteoporosis - DXA at 1-2 years

身體與心智功能衰退：心血管疾病、糖尿病、高血壓、癌症、憂鬱症

年齡增長自然老化



增加活動量

打破惡性循環

體能衰退

免疫功能下降

社會觀念

“靜享清福”

活動量下降