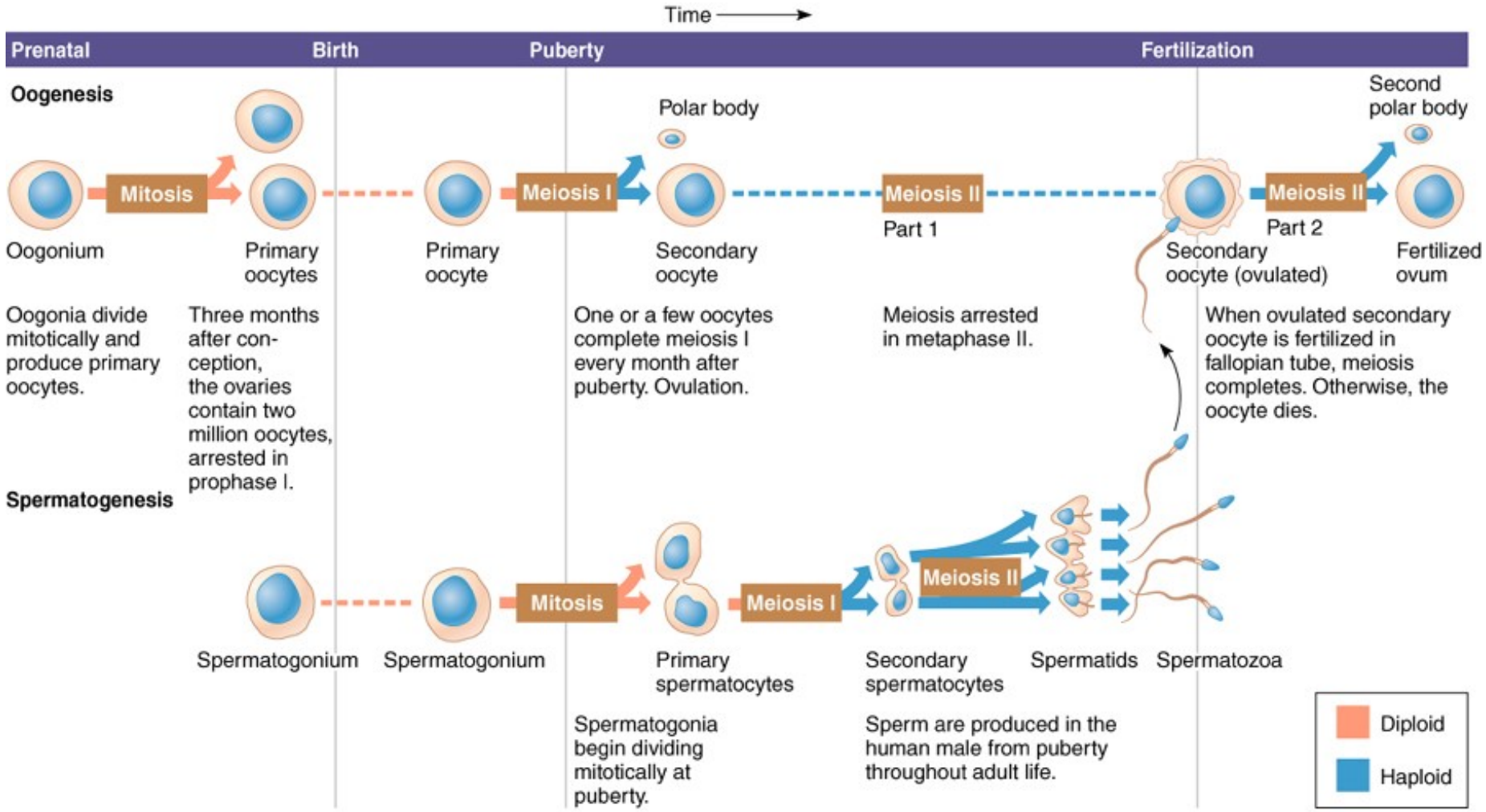
Funzione gametogenica

Comparison of Oogenesis and Spermatogenesis



1. *Strutture testicolari coinvolte nella spermatogenesi*

2. *Controllo della spermatogenesi*

   I. controllo endocrino

   II. controllo paracrino

   III. integrazione dei meccanismi di controllo

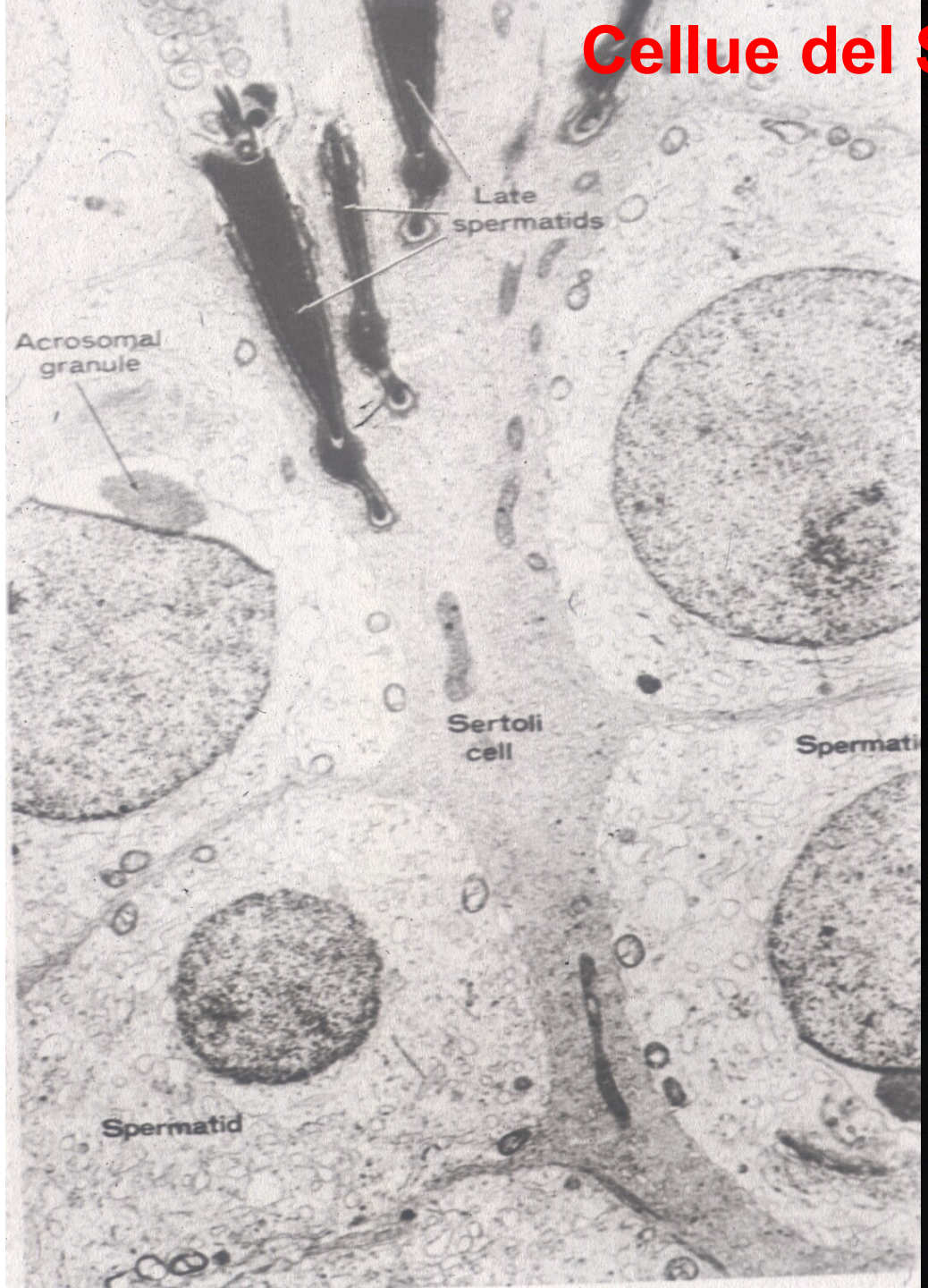
Cellue del Sertoli

- Le cellule del Sertoli si differenziano costituendo la barriera ematotesticolare ed il fluido tubulare.

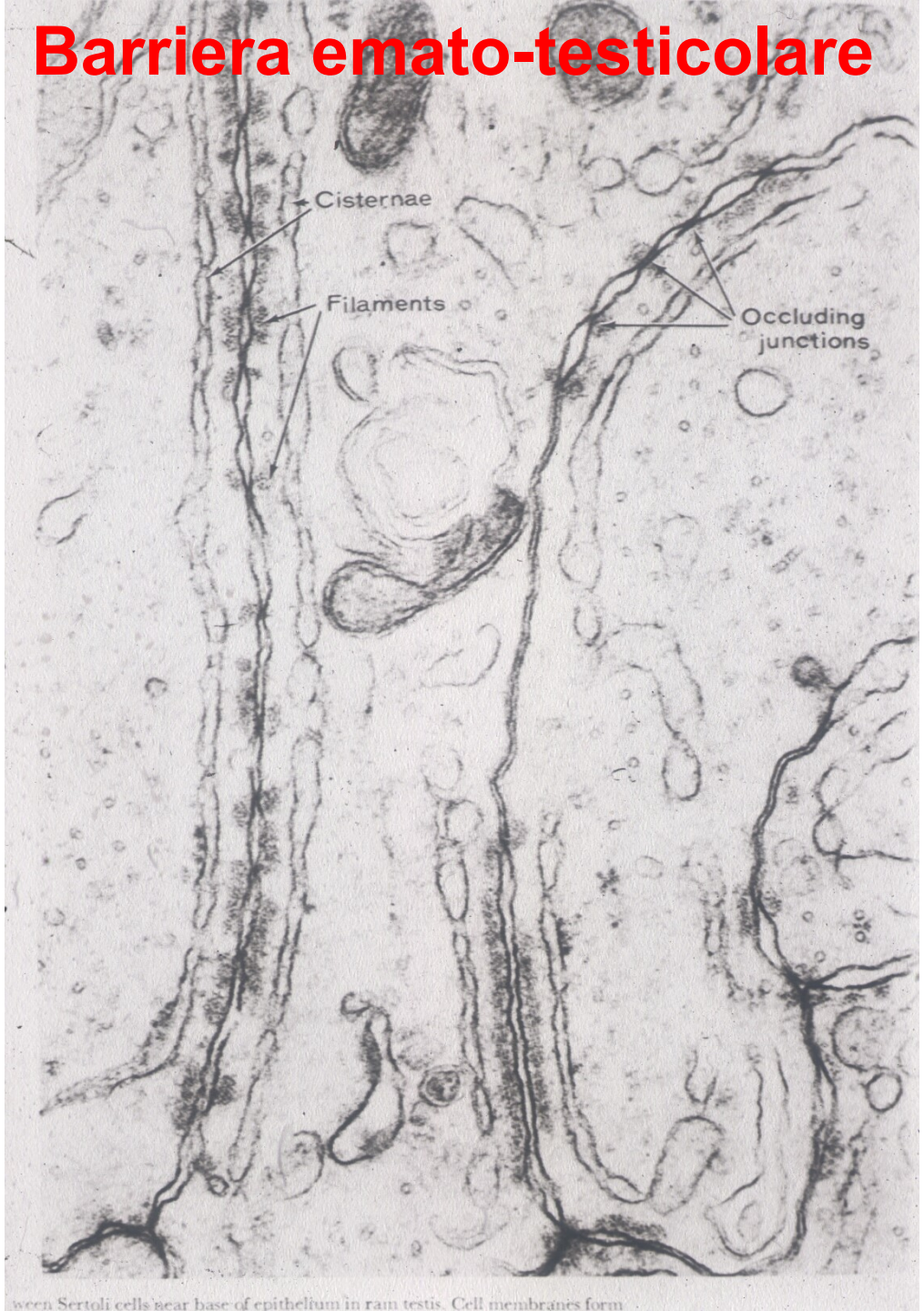
- Dopo la pubertà non si hanno più mitosi, per cui le cellule non possono essere rimpiazzate.

- Popolazioni stabili grazie all'espresione del gene antiapoptotico *Bclw*.

Cellue del Sertoli



Barriera emato-testicolare



ween Sertoli cells near base of epithelium in ram testis. Cell membranes form

apoptosi

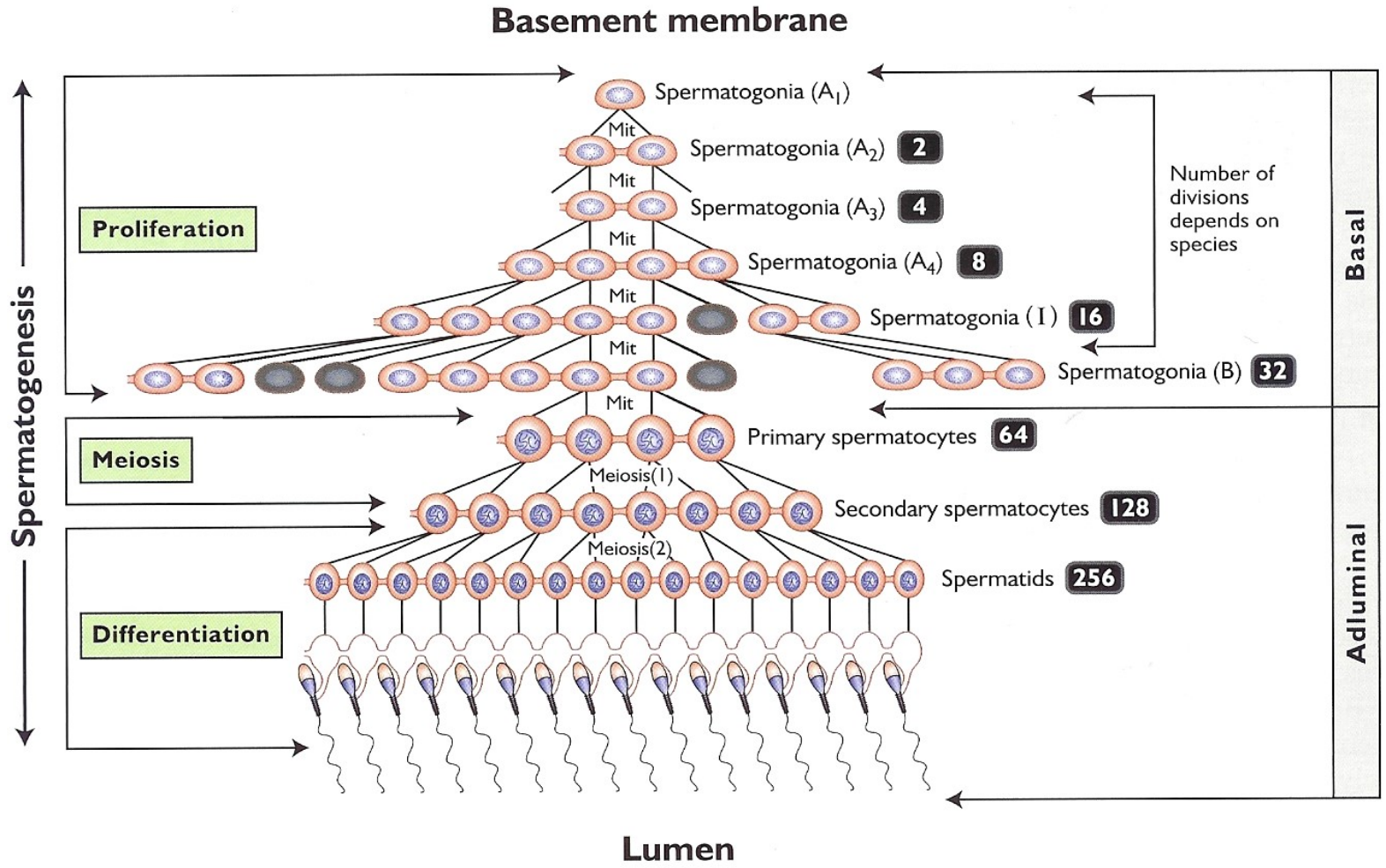
SPERMATOGENESI

La spermatogenesi riconosce tre fasi:

1. Fase spermatogonica (proliferativa o mitotica)
2. Fase spermatocitaria (meiotica)
3. Fase spermiogenica (differenziativa)

Figure 10-5. Typical Sequence of Spermatogenesis in Mammals

Spermatogonia (A_1-A_4, I and B) undergo a series of mitotic divisions (Mit) and the last mitotic division gives rise to primary spermatocytes that enter meiosis. This series of mitotic divisions allows for continual proliferation of spermatogonia and replacement of A_1 spermatogonia.



After meiosis, haploid spherical spermatids differentiate into spermatozoa. Meiosis and differentiation take place in the adluminal compartment. Notice that each generation of cells is attached by intercellular cytoplasmic bridges. Thus, each generation divides synchronously in cohorts. Some cells (black) degenerate during the process. Numbers indicate the theoretical number of cells generated by each division.

Fase spermatogonica

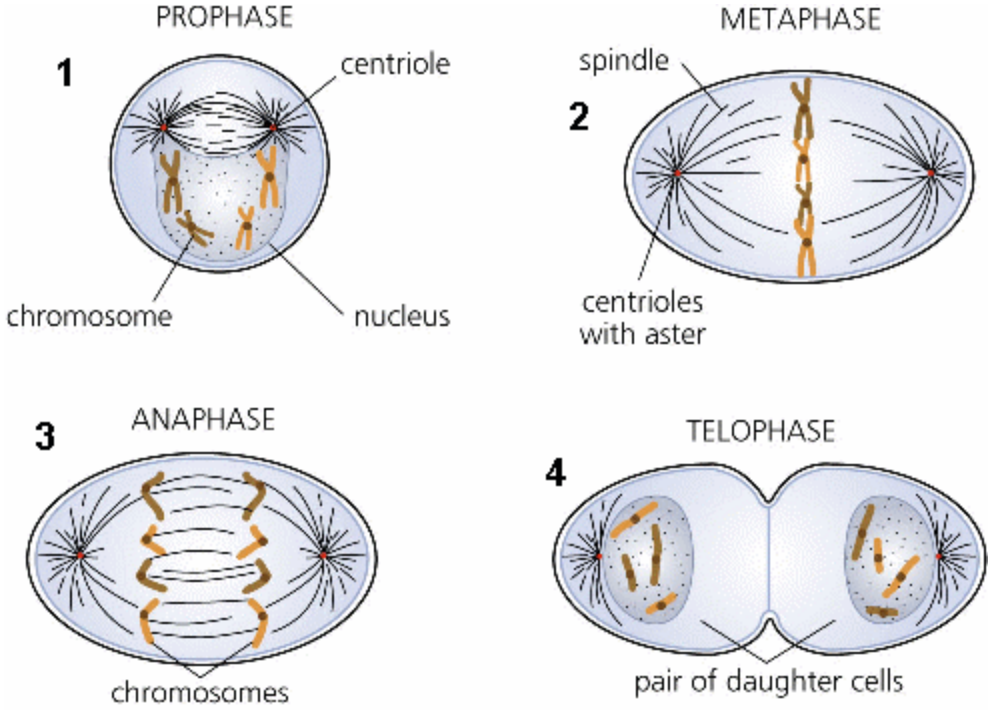
Detta anche spermatocitogenesi, è la fase in cui si ha la proliferazione delle cellule staminali per dare diverse generazioni di spermatogoni (sparmatogoni A).

L’ultima generazione di cellule goniali, che andrà incontro alla fase successiva, è costituita dagli spermatogoni B.

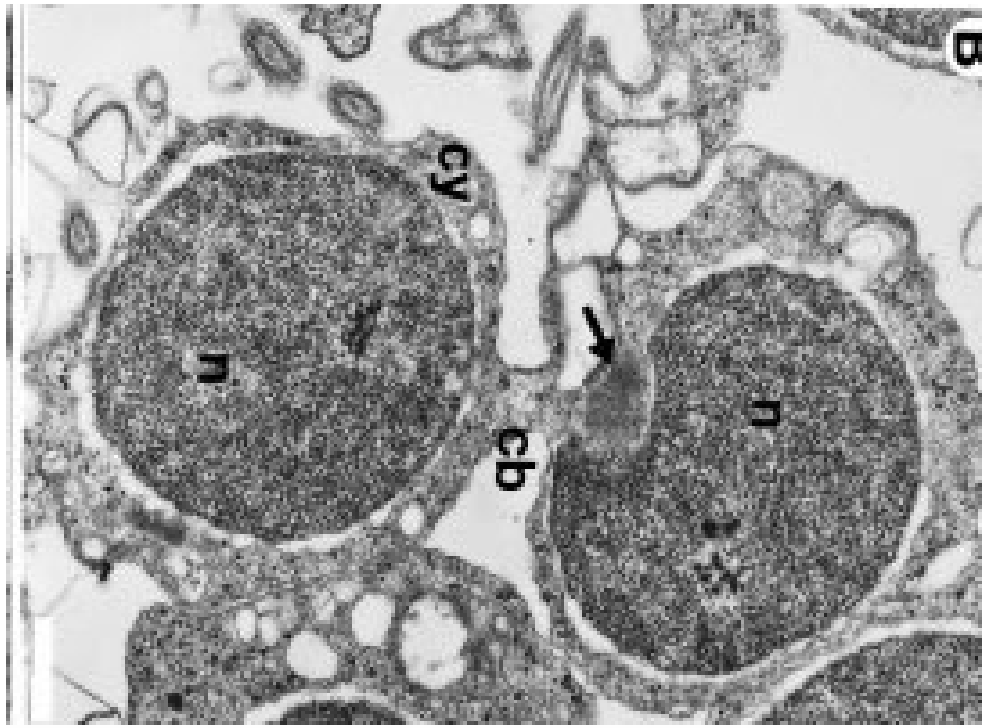
Spermatogoni A

- Nucleo sferico o ellittico con uno o due nucleoli.
- Citoplasma omogeneo e poco colorato.
- Esistono spermatogoni A con nucleoplasma scuro ed un grosso vacuolo pallido (detti “scuri”)

Possono rimanere quiescenti per un lunghissimo periodo di tempo e poi dividersi per produrre altri goni di tipo A.



Durante tutte le divisioni successive alle prime divisioni goniali, la citodieresi rimane incompleta e si formano clusters di cellule figlie unite da ponti citoplasmatici.



Spermatogoni B

- Nucleo sferico, con zolle di cromatina, con un solo nucleolo centrale.

- Citoplasma simile a spermatogoni A.

Spermatociti

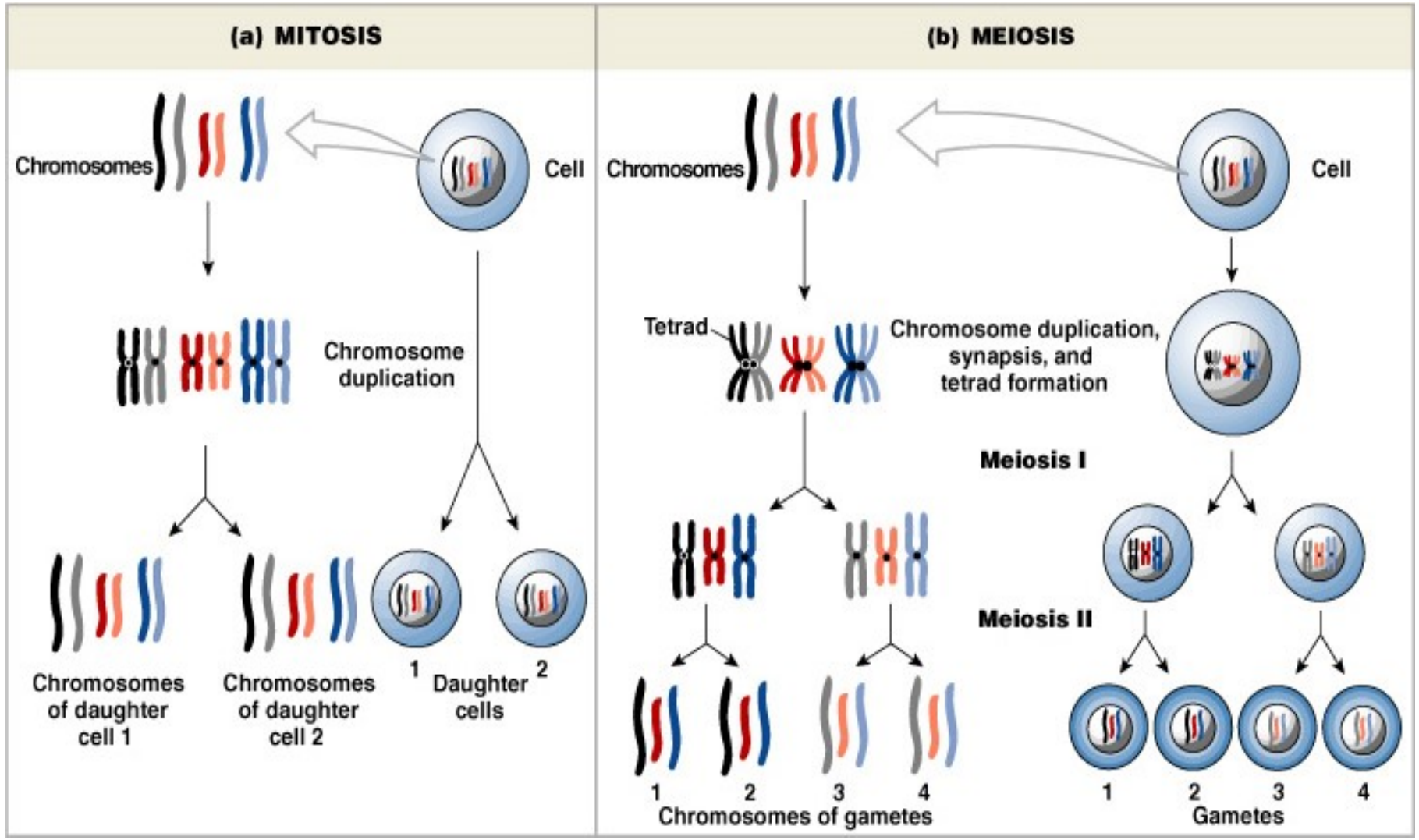
Inizialmente somigliano agli spermatogoni B da cui derivano, successivamente procedono verso il lume tubulare e si arricchiscono di citoplasma.

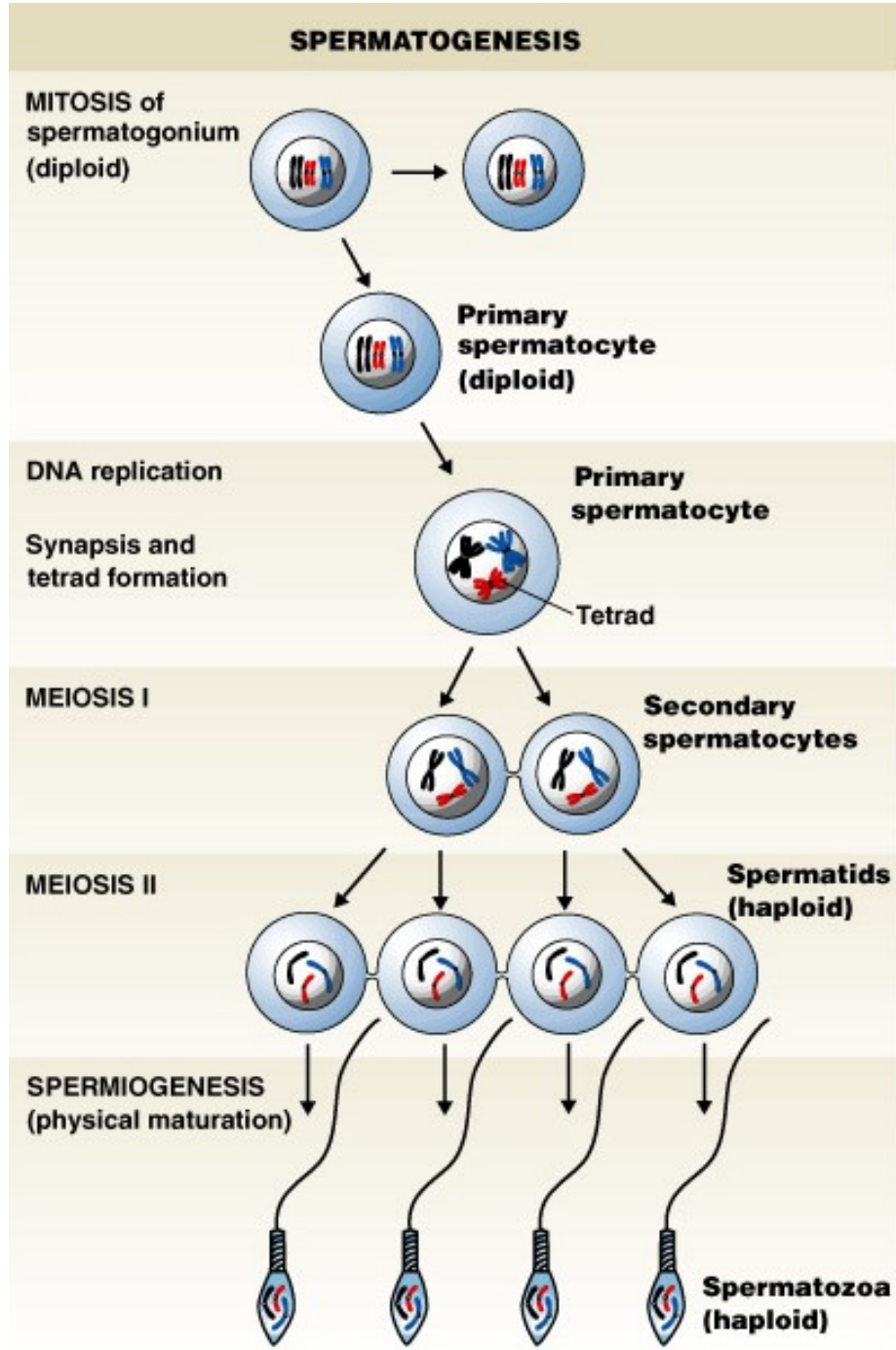
Appena formatisi iniziano la profase della MEIOSI.

Fase meiotica

Gli spermatociti vanno incontro a mitosi e diventano da 2n → n.

mitosi e meiosi

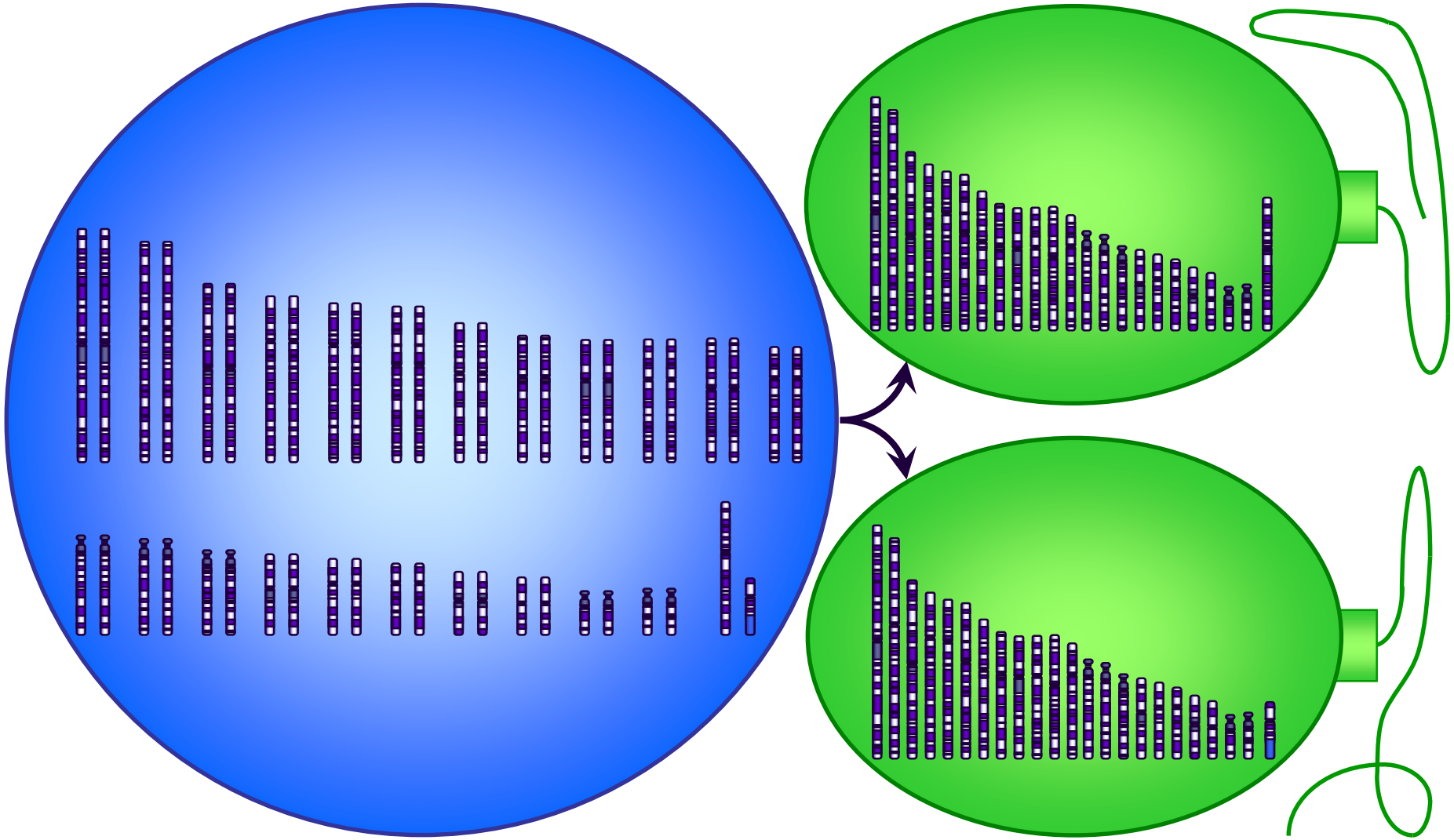



SPERMATOGENESIS
MITOSIS of spermatogonium (diploid)
Primary spermatocyte (diploid)
DNA replication
Synapsis and tetrad formation
Primary spermatocyte
Tetrad
MEIOSIS I
Secondary spermatocytes
MEIOSIS II
Spermatids (haploid)
SPERMIOGENESIS (physical maturation)
Spermatozoa (haploid)

La profase dura moltissimo, nell’uomo circa 22 giorni.

E’ il momento in cui si determina il sesso dello spermatozoo.

Spermatogenesis



Fase spermioistogenetica

Da spermatidi a spermatozoi differenziati

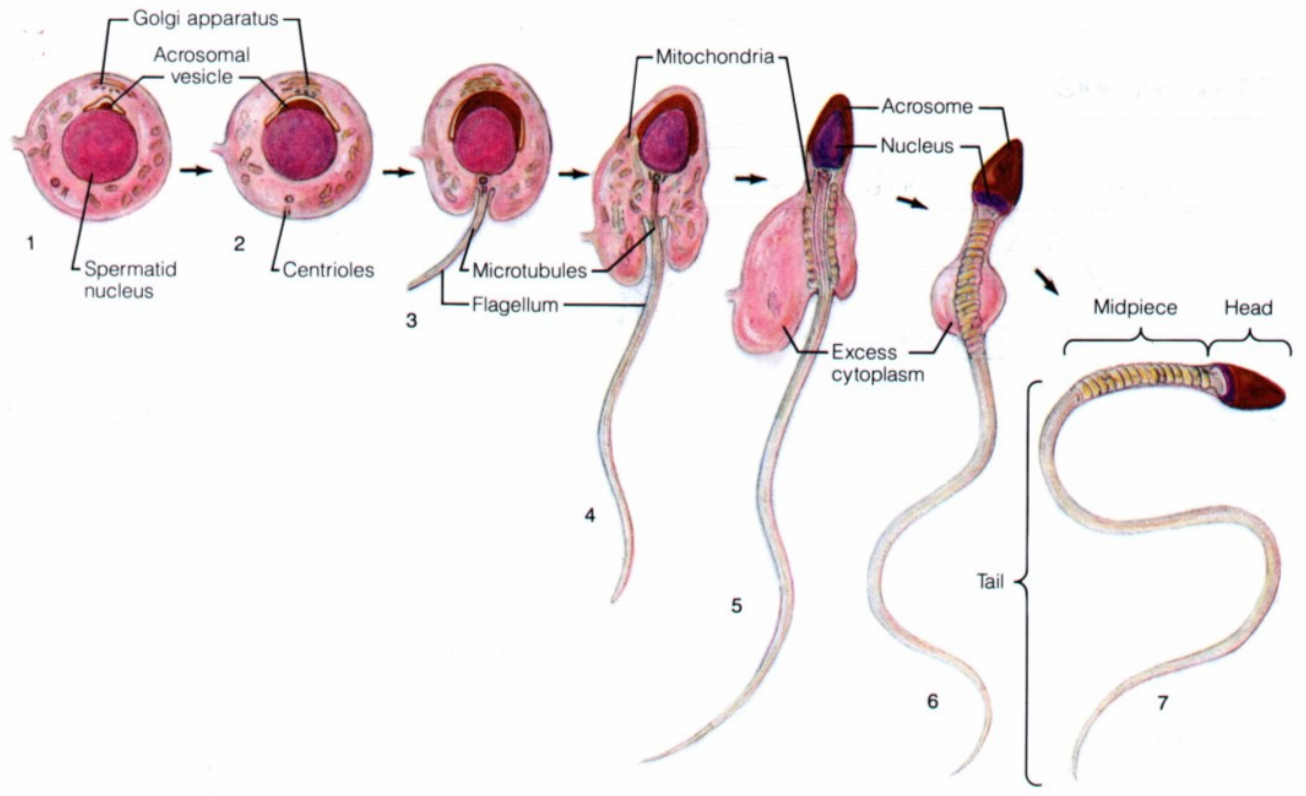
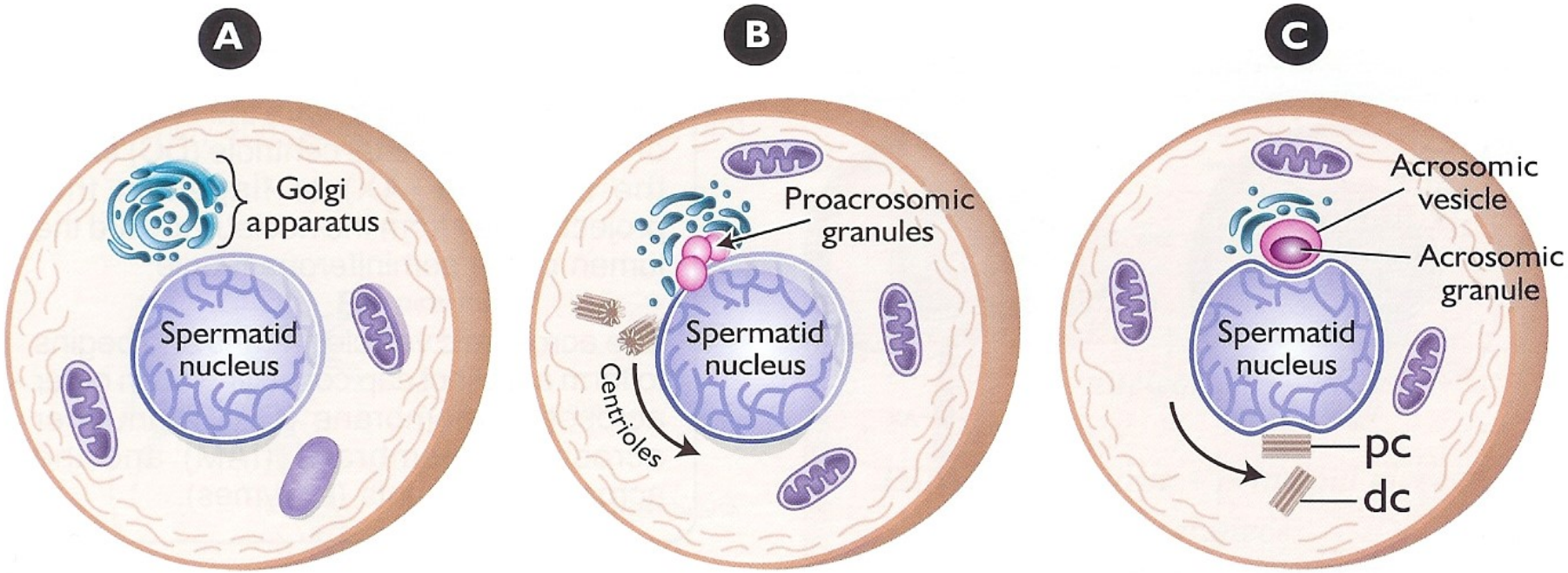


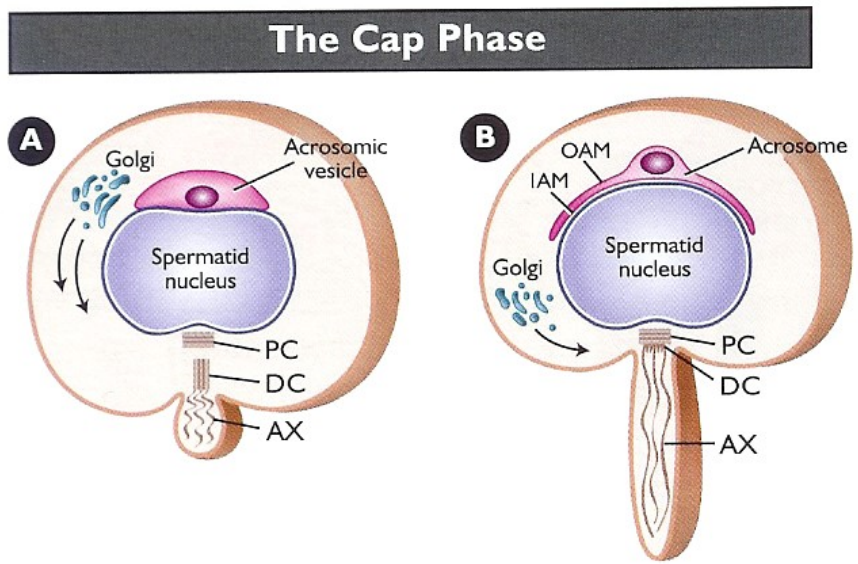
Figure 10-6. The Golgi Phase of Spermatid Differentiation



The newly formed spermatid is almost perfectly spherical and has a well developed Golgi apparatus.

Small vesicles of the Golgi fuse, giving rise to larger secretory granules called pro-acrosomic granules. The centrioles start to migrate to a position beneath the nucleus that is opposite the acrosomic vesicle.

Vesicle fusion continues until a large acrosomic vesicle is formed that contains a dense acrosomic granule. The proximal centriole (PC) will give rise to the attachment point of the tail. The distal centriole (DC) will give rise to the developing axoneme (central portion of the tail) inside the cytoplasm of the spermatid.

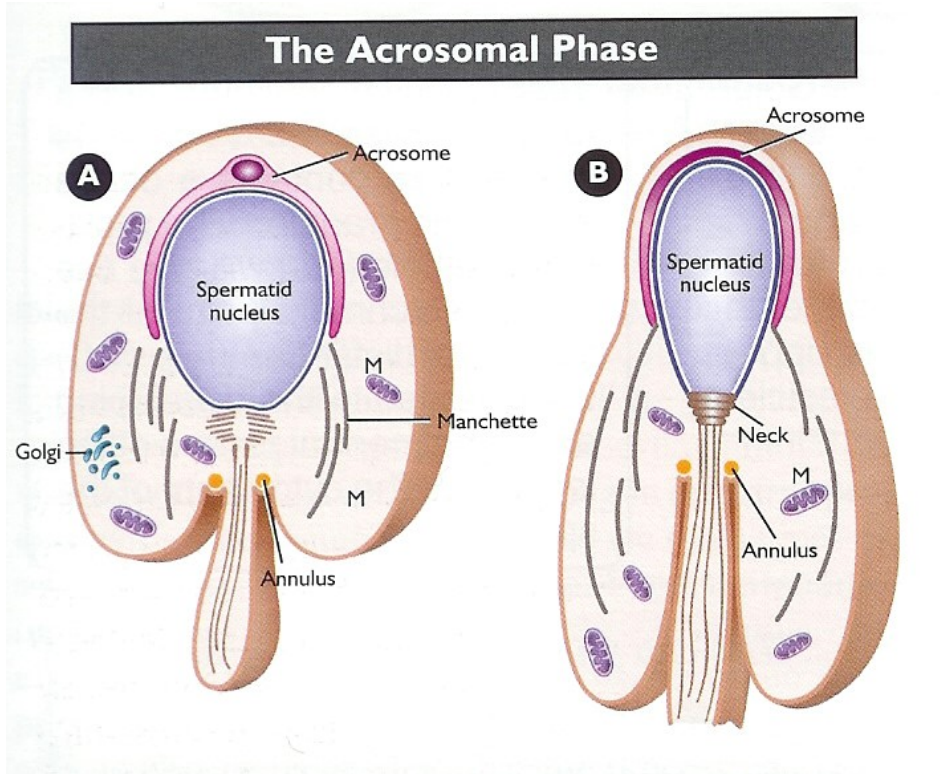


A

The Golgi migrates toward the caudal part of the cell. The distal centriole (DC) forms the axoneme (AX) or flagellum that projects away from the nucleus toward the lumen of the seminiferous tubule.

B

The acrosomic vesicle flattens and begins to form a distinct cap consisting of an outer acrosomal membrane (OAM), an inner acrosomal membrane (IAM) and the acrosomal contents (enzymes).

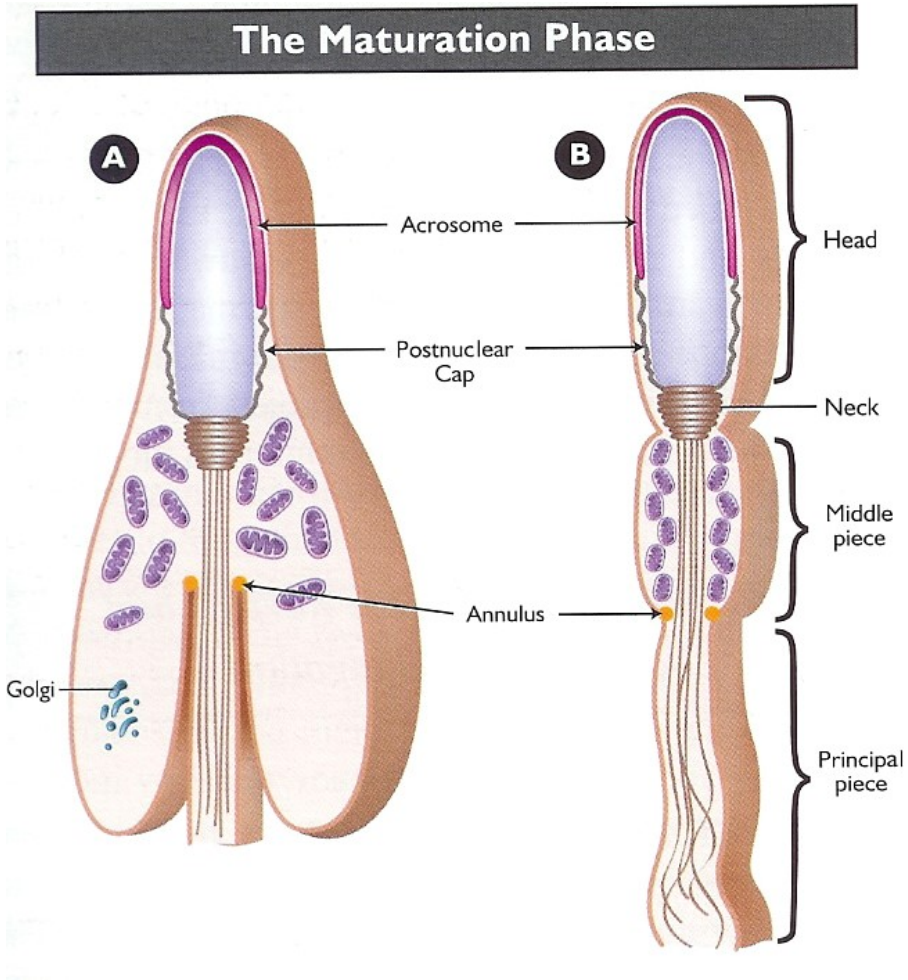


A

The spermatid nucleus begins to elongate and the acrosome eventually covers the majority of the anterior nucleus. The manchette forms in the region of the caudal half of the nucleus and extends down toward the developing flagellum.

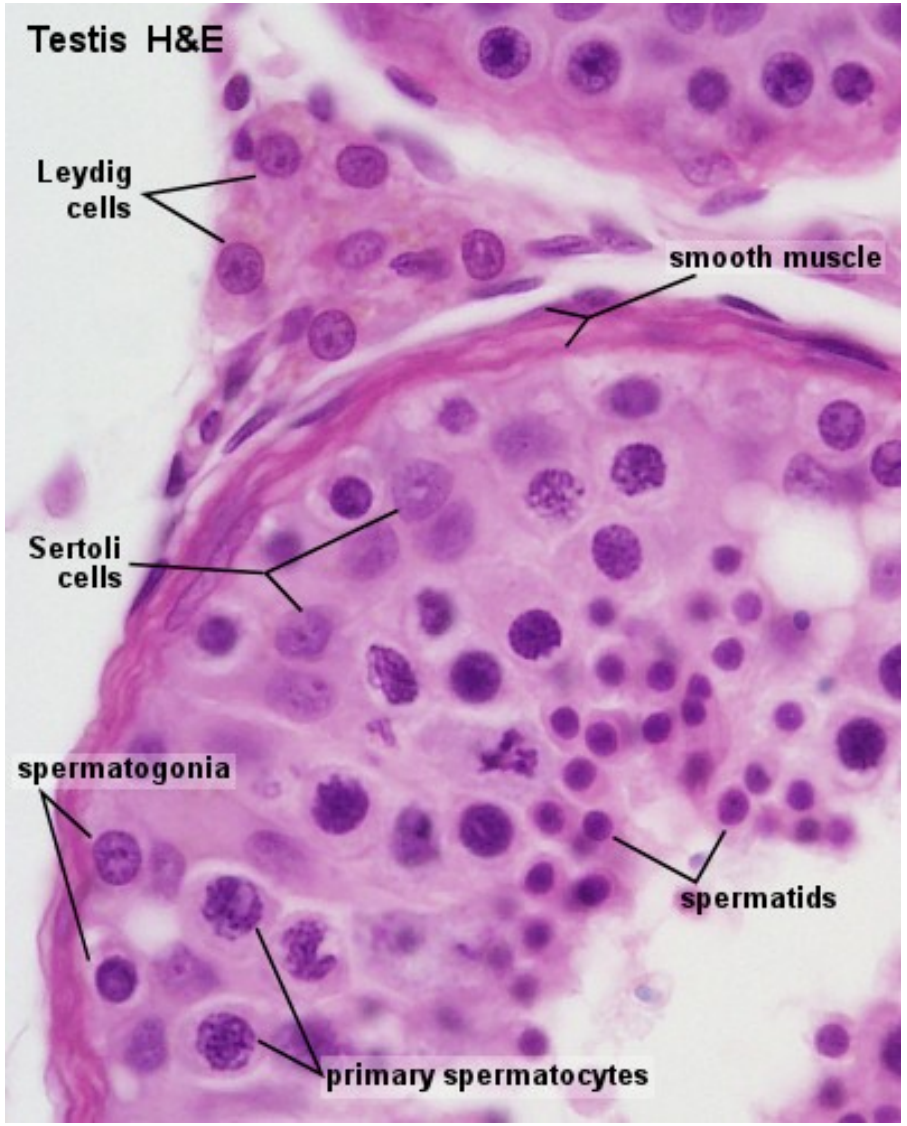
B

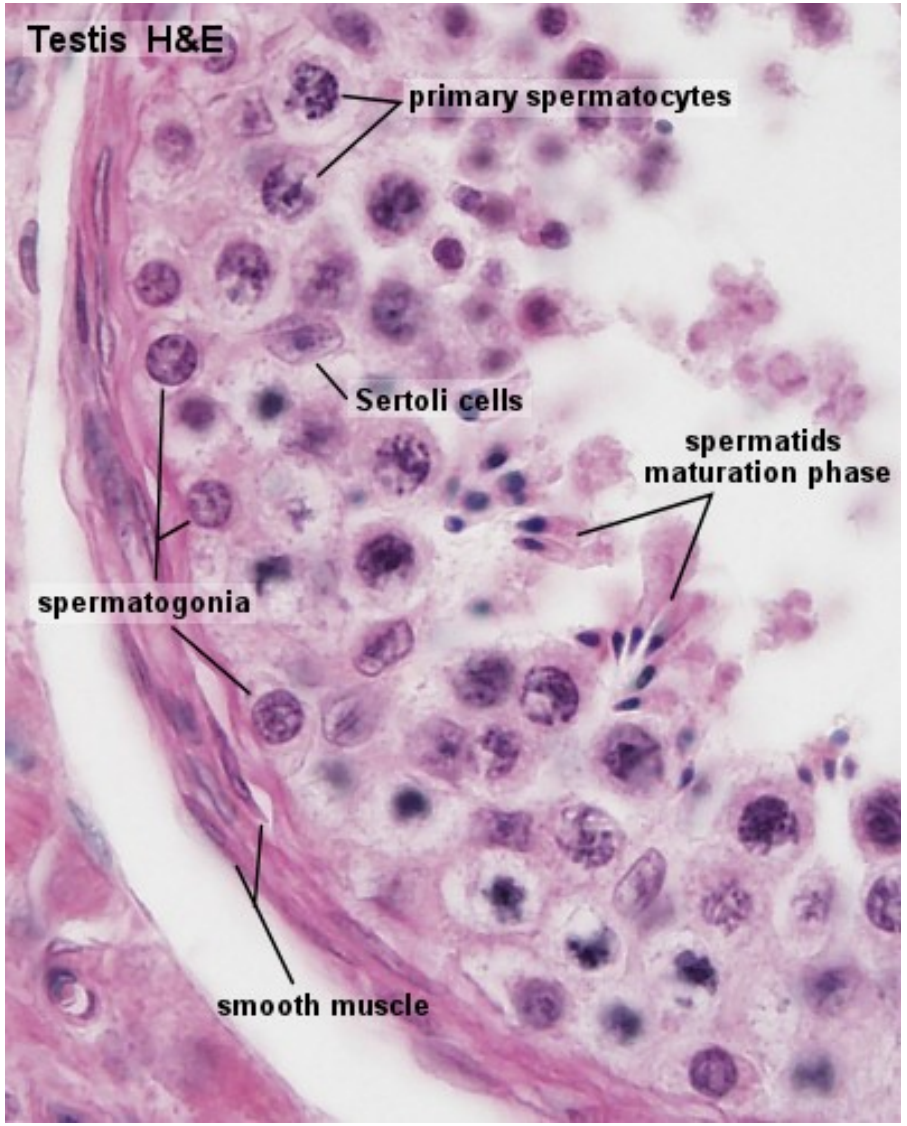
The neck and the annulus are formed and the later will become the juncture between the middle piece and the principal piece. Notice that all components of the developing spermatid are completely surrounded by a plasma membrane. M = mitochondria.



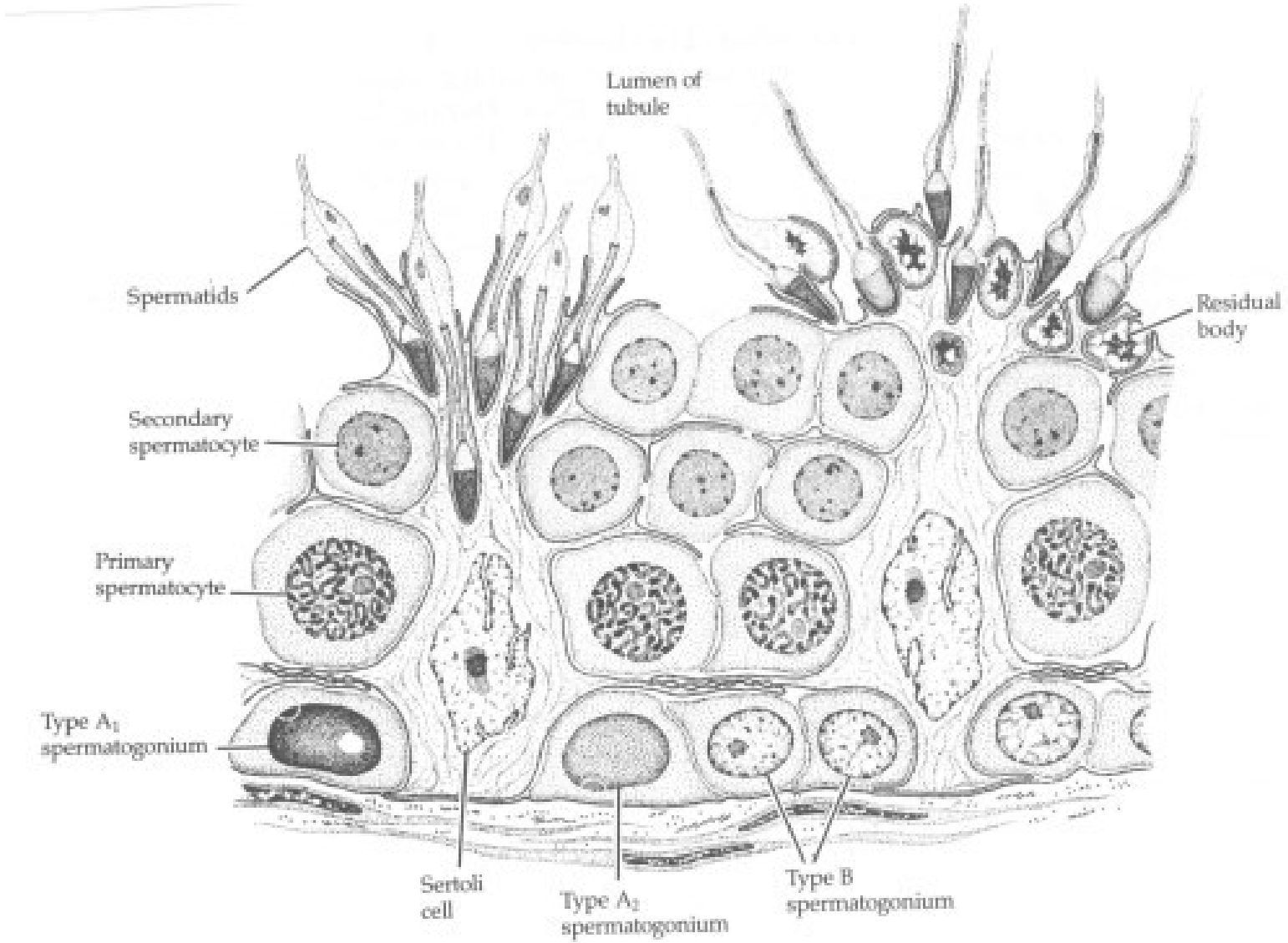
A and B

Mitochondria form a spiral assembly around the flagellum that defines the middle piece. The postnuclear cap is formed from the manchette microtubules. The annulus forms the juncture between the middle piece and the principal piece.

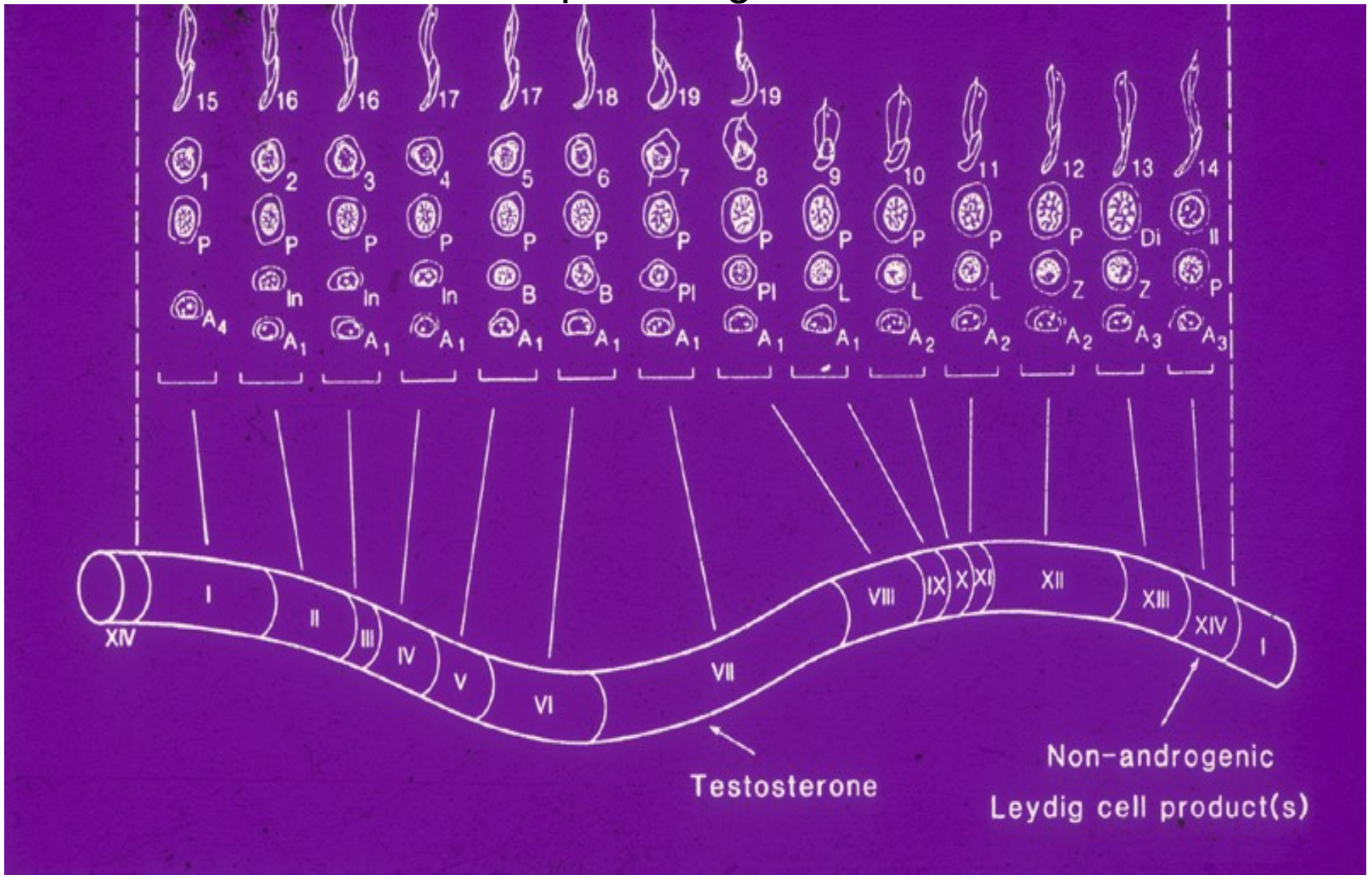

Testis H&E
Leydig cells
smooth muscle
Sertoli cells
spermatogonia
spermatids
primary spermatocytes

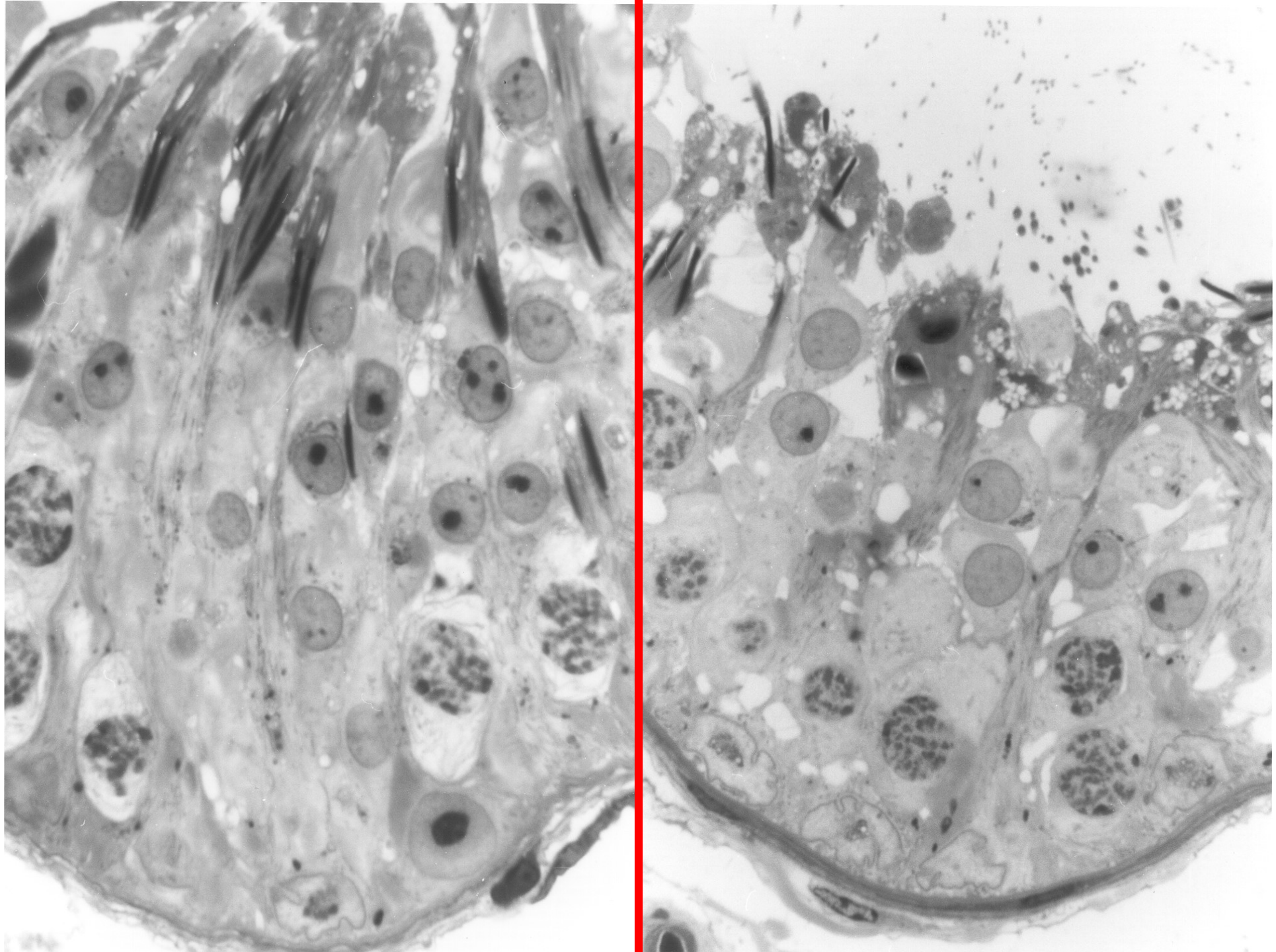

Testis H&E
primary spermatocytes
Sertoli cells
spermatids maturation phase
spermatogonia
smooth muscle

CICLO EPITELIO SEMINIFERO



The Spermatogenic Wave





Durata della spermatogenesi

	toro	ariete	verro	stallone	uomo
giorni	61	47	39	57	75

RIMODELLAMENTO NUCLEARE

Le protamine

Nei mammiferi sono presenti:

- P1
- famiglia P2 (P2, P3, P4)

Si tratta di proteine caratterizzate da un elevato contenuto di residui di arginina (48% nell'uomo).

Funzioni delle protamine

I: condensare la cromatina paterna, per rendere il nucleo più compatto ed idrodinamico.

II: proteggere il DNA rendendolo inaccessibile all'azione delle nucleasi e di agenti mutageni.

III: rendere più agevole la riprogrammazione nucleare all'oocita.

Funzioni delle protamine

IV: conferire un particolare “epigenetic mark” a specifiche regioni del genoma paterno

V: il rimaneggiamento nucleare rappresenta un ceckpoint durante la spermatogenesi

VI: potrebbero avere un ruolo durante o dopo la fecondazione

Transizione nucleoistone-nucleoprotamine

La prime fasi del rimodellamento nucleare consistono nella incorporazione di particolari istoni.

Successivamente si ha l'iperacetilazione degli istoni.

Segue il rilassamento della cromatina e l'esposizione dei siti per il legame di varie proteine

Transizione nucleoistone-nucleoprotamine

In particolare si ha il legame di bromodomain-containing protein (BRDT) all'istone H4 iperacetilato.

Contemporaneamente il DNA viene complessato dalle TNPs, che poi verranno sostituite dalle protamine. Durante la condensazione della cromatina di ha una defosforilazione di tali proteine.

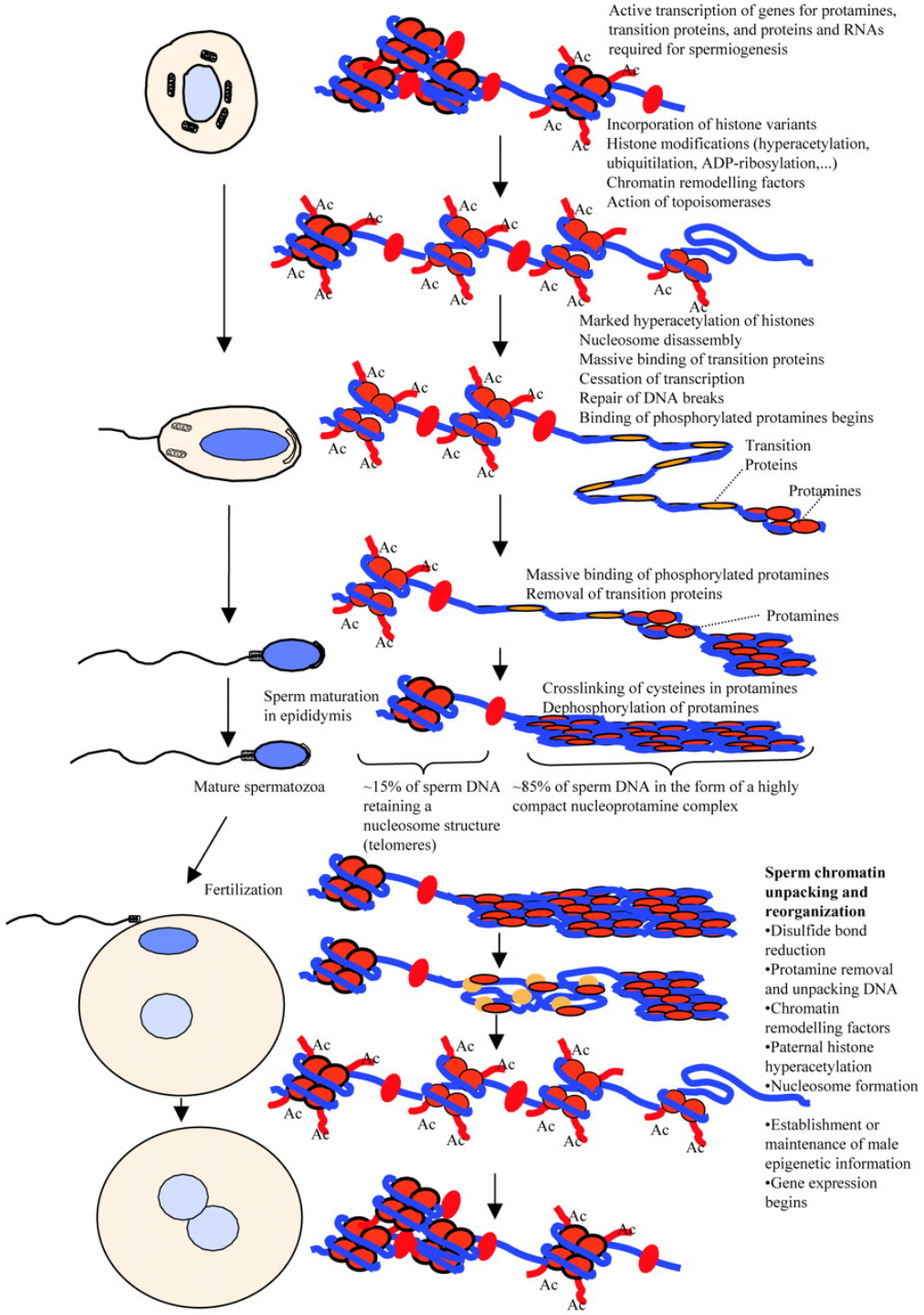
Man mano che la spermatogenesi prosegue i complessi di nucleoprotamine vengono stabilizzati da ponti disolfuro

Organizzazione del DNA dello spermatozoo

Circa l’85% del DNA è organizzato come complesso di nucleoprotamine.

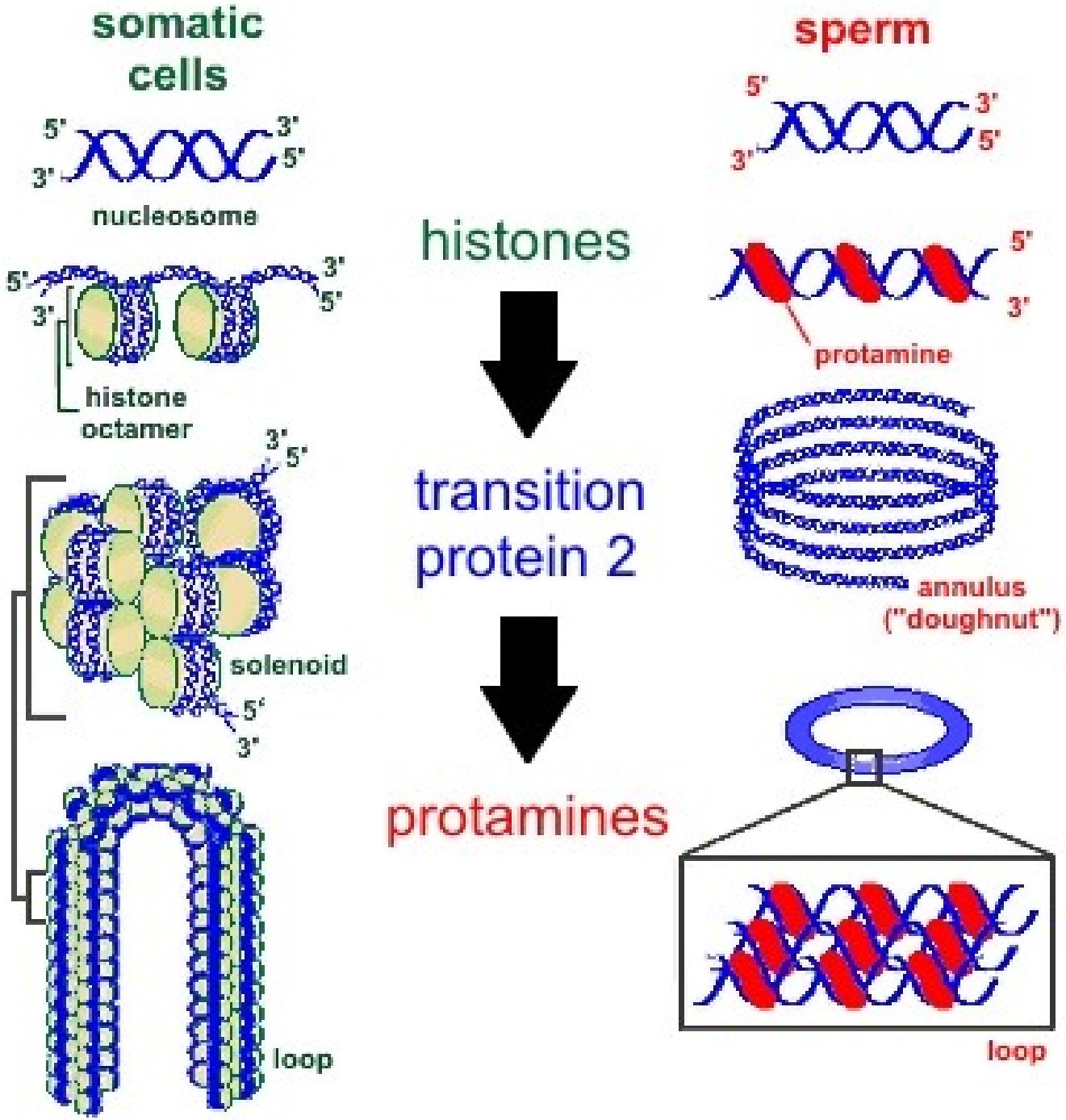
Il rimanente 15% è associato ad istoni o ad altre proteine

Inoltre i centromeri son disposti in posizione profonda, mentre i telomeri, associati a formare dimeri, sono disposti alla periferia



The round spermatid (top left) has a chromatin structure similar to that present in all somatic cells, with the DNA organized in nucleosomes and many genes being actively transcribed. During the initial stages of spermiogenesis, histones are hyperacetylated and undergo other modifications, nucleosomes are disassembled, topoisomerase II unwinds superhelicity of the DNA, transcription ceases and transition proteins (TNPs) bind the DNA. At the final stage of spermiogenesis, TNPs are removed and protamines progressively bind the DNA. During sperm maturation in the epididymis, the formation of disulphide bonds in protamines further stabilizes the nucleoprotamine complex. At fertilization, the highly compact nucleoprotamine structure must be unpacked and reorganized into a nucleosomal structure. Histones are represented in red and DNA is represented by blue lines. The presence of hyperacetylation in the N-terminal histone tails is indicated by ‘Ac’. Transition proteins are represented as orange elongated ovals. Protamines are represented as red elongated ovals.

Oliva R. Human Reproduction Update 12; 417-435, 2006


somatic cells
5'
3'
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nucleosome
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histone octamer
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solenoid
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loop
histones
transition protein 2
protamines
sperm
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protamine
annulus ("doughnut")
loop