Dipartimento
di Salute della Donna e del Bambino - SDB

Clinica Ginecologica e Ostetrica

Direttore: Prof. Giovanni B. Nardelli

I^ Lezione : Gametogenesi - Fecondazione - Placentazione - Funzioni Placentari

La GAMETOGENESI
è il processo che porta alla formazione dei GAMETI

Cellula Diploide (2n)

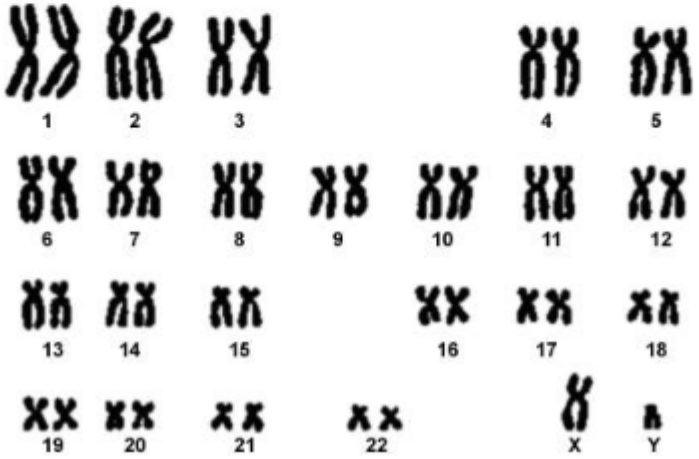
Cellula che contiene coppie di cromosomi omologhi (un set materno e uno paterno)

Cellula Aploide (n)

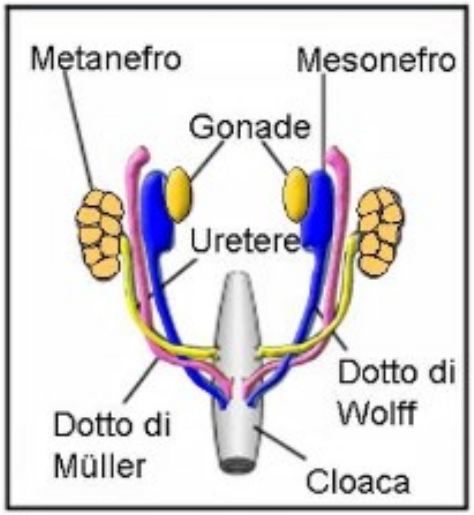
Cellula che contiene un solo rappresentante di ciascuna coppia di cromosomi omologhi

Cariotipo umano → 23 (n) + 23 (n) = 46 cromosomi (2n)

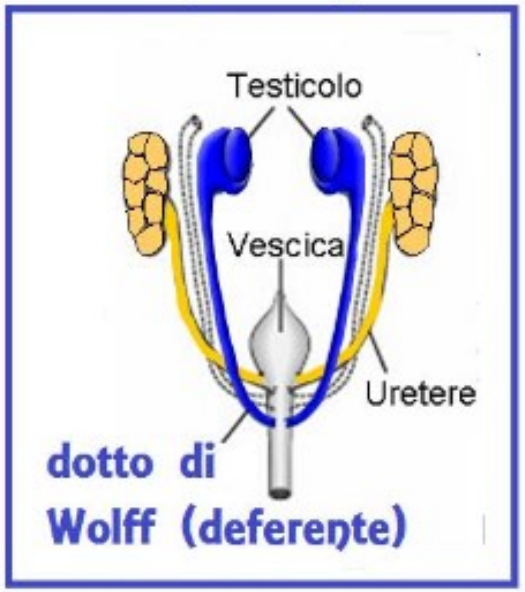
(Corredo genomico)



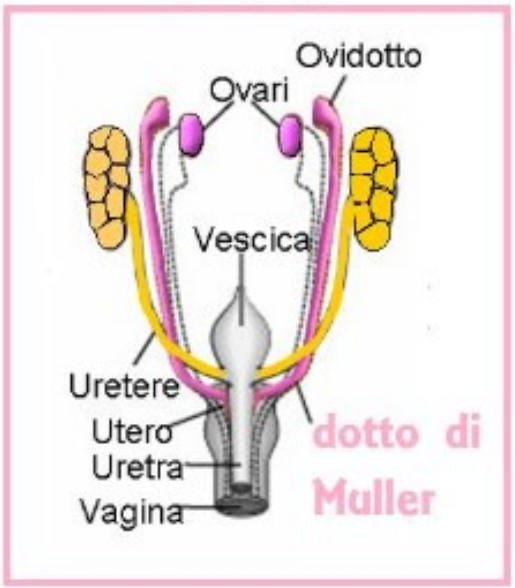
Stadio neutro (<8 w)



maschio

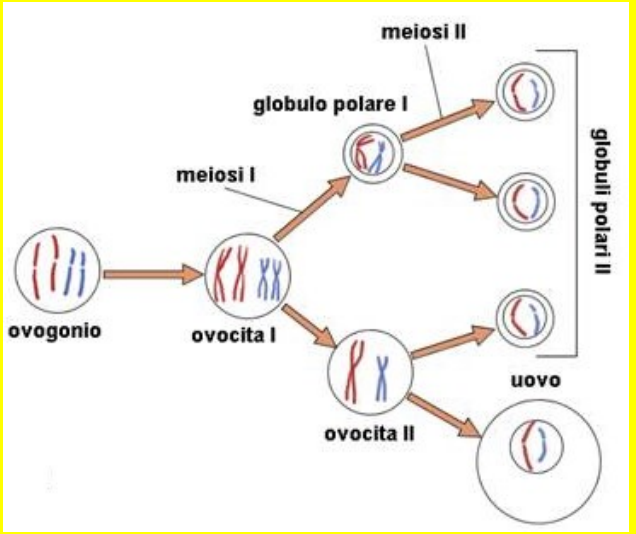


femmina



CICLO CELLULARE

nella Fisiopatologia della Riproduzione Umana



Esistono due tipi di divisione cellulare:
MEIOSI e MITOSI

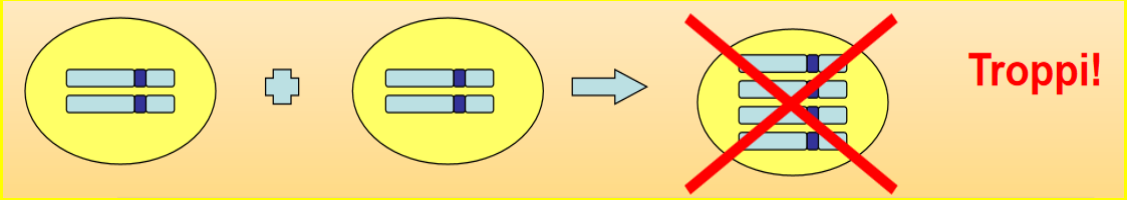
Meiosi (cellule germinali)

la Meiosi genera la diversità genetica

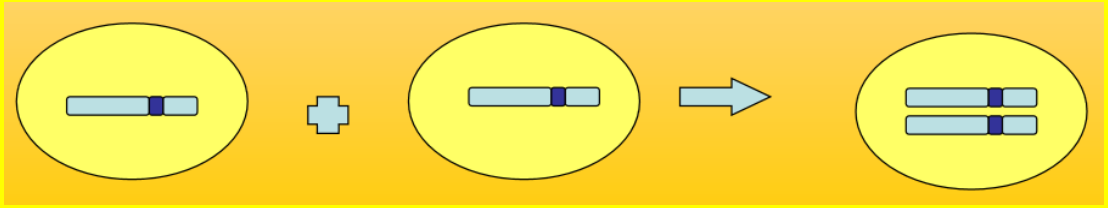
Da 1 cellula eucariota con corredo cromosomico diploide
prendono origine 4 cellule con corredo cromosomico aploide.

LO SCOPO DELLA MEIOSI
è la
riduzione del materiale genetico nei gameti

Dalla madre Dal padre Figlio



La meiosi riduce materiale genetico nei gameti maturi



MEIOSI

E' il processo per mezzo del quale si originano le cellule sessuali
i **gameti maschili** e i **gameti femminili**

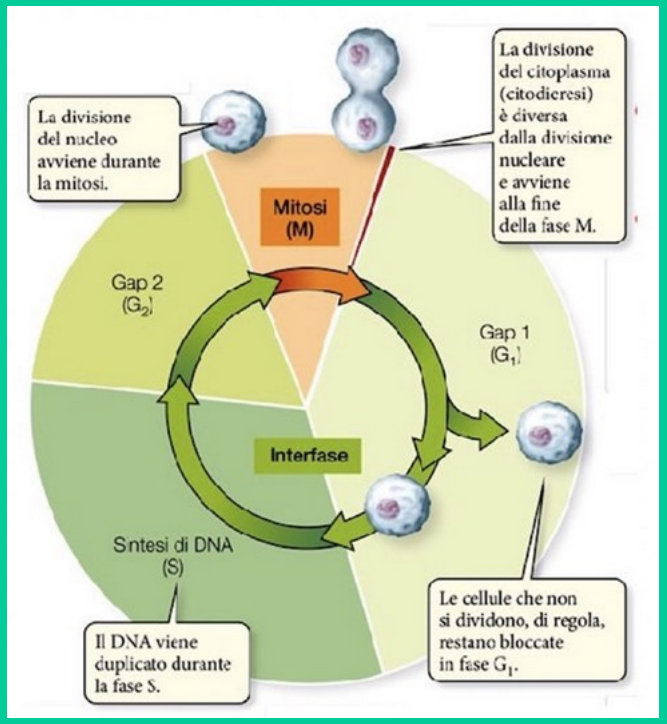
Si dimezza il numero dei cromosomi
da *diplode* (46, o 2*n*)
ad *aploide* (23, o *n*)

Il concepimento ricostituisce il numero diploide dell' uovo fecondato (***zigote***)

CICLO CELLULARE

nella Fisiopatologia della Riproduzione Umana

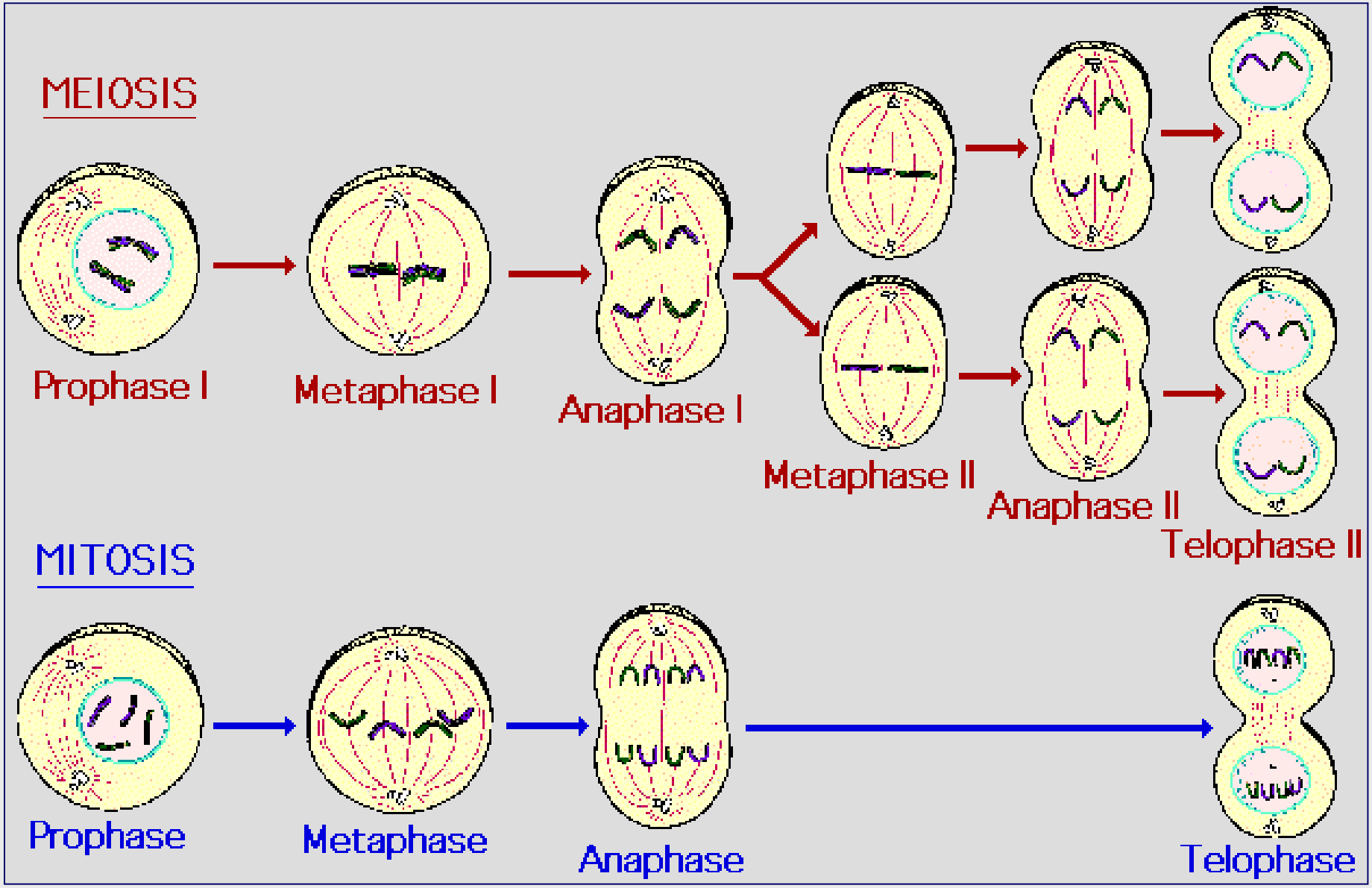
Esistono due tipi di <u>divisione cellulare</u>:
MEIOSI e MITOSI



Mitosi (cellule somatiche)

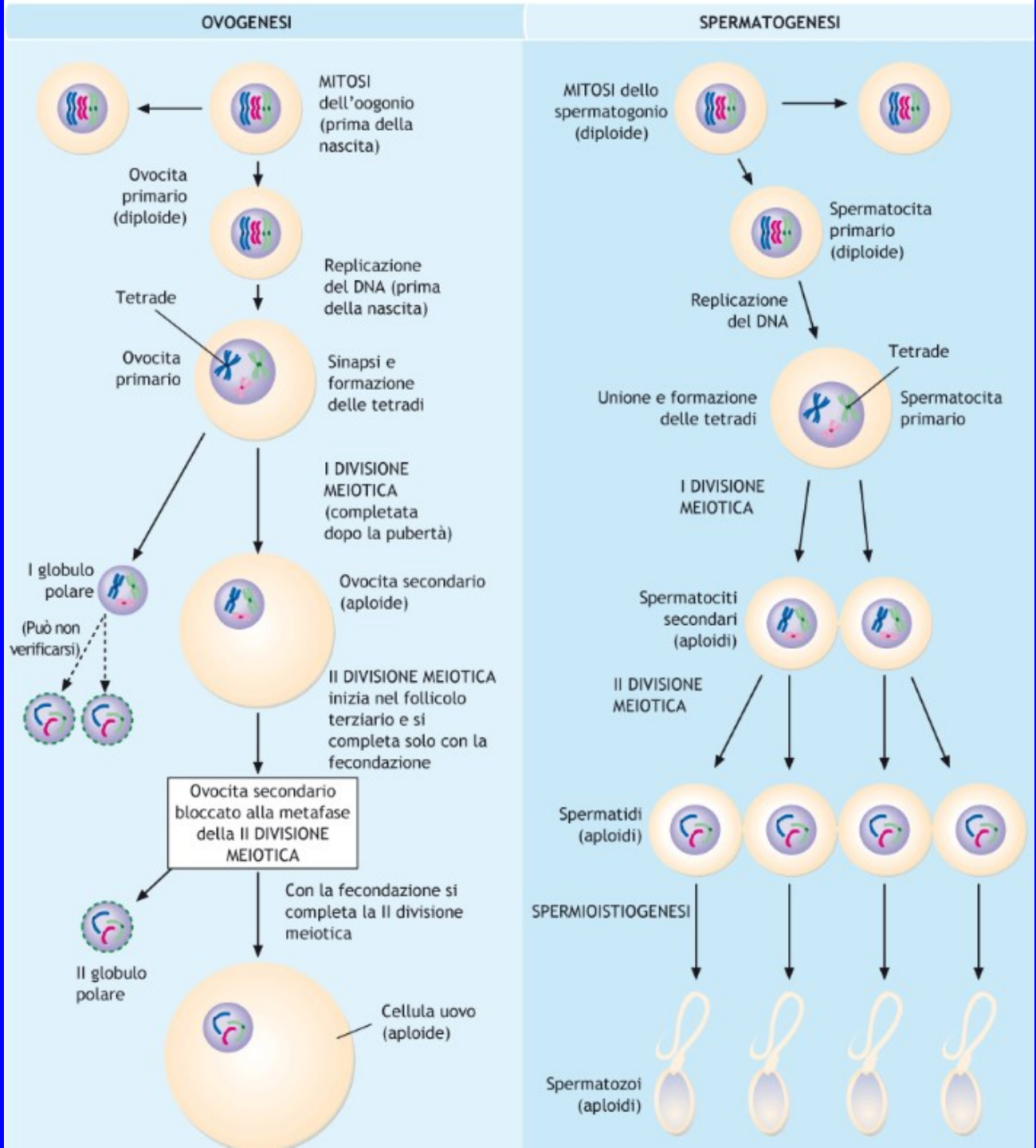
La riproduzione di una cellula somatica (**mitosi**) ha lo scopo di trasmettere l'informazione genetica alle cellule figlie in modo che abbiano le stesse caratteristiche e le stesse funzioni della cellula genitrice

Le cellule figlie, *risultanti da questa divisione,*
sono identiche alla cellula genitrice


MEIOSIS
Prophase I
Metaphase I
Anaphase I
Metaphase II
Anaphase II
Telophase II
MITOSIS
Prophase
Metaphase
Anaphase
Telophase

GAMETOGENESI nella femmina e nel maschio

2 tipi di divisione cellulare:
Mitosi (cellule somatiche)
Meiosi (cellule germinali)



Esistono due tipi di <u>divisione cellulare</u>:
Mitosi (cellule somatiche)
Meiosi (cellule germinali)

spermatogenesi 1

spermatogonio Ad

mitosi

spermatogonio Ad

spermatogoni Ap

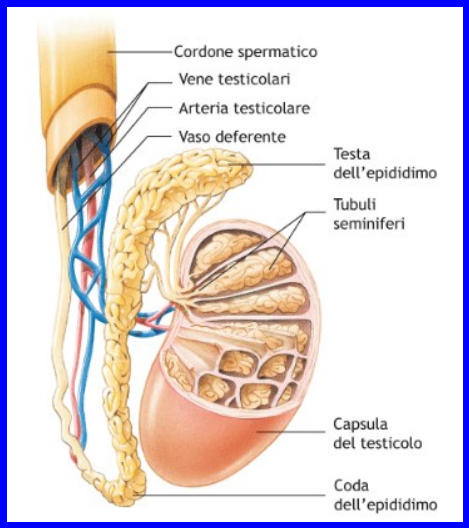
mitosi

spermatogoni B

mitosi

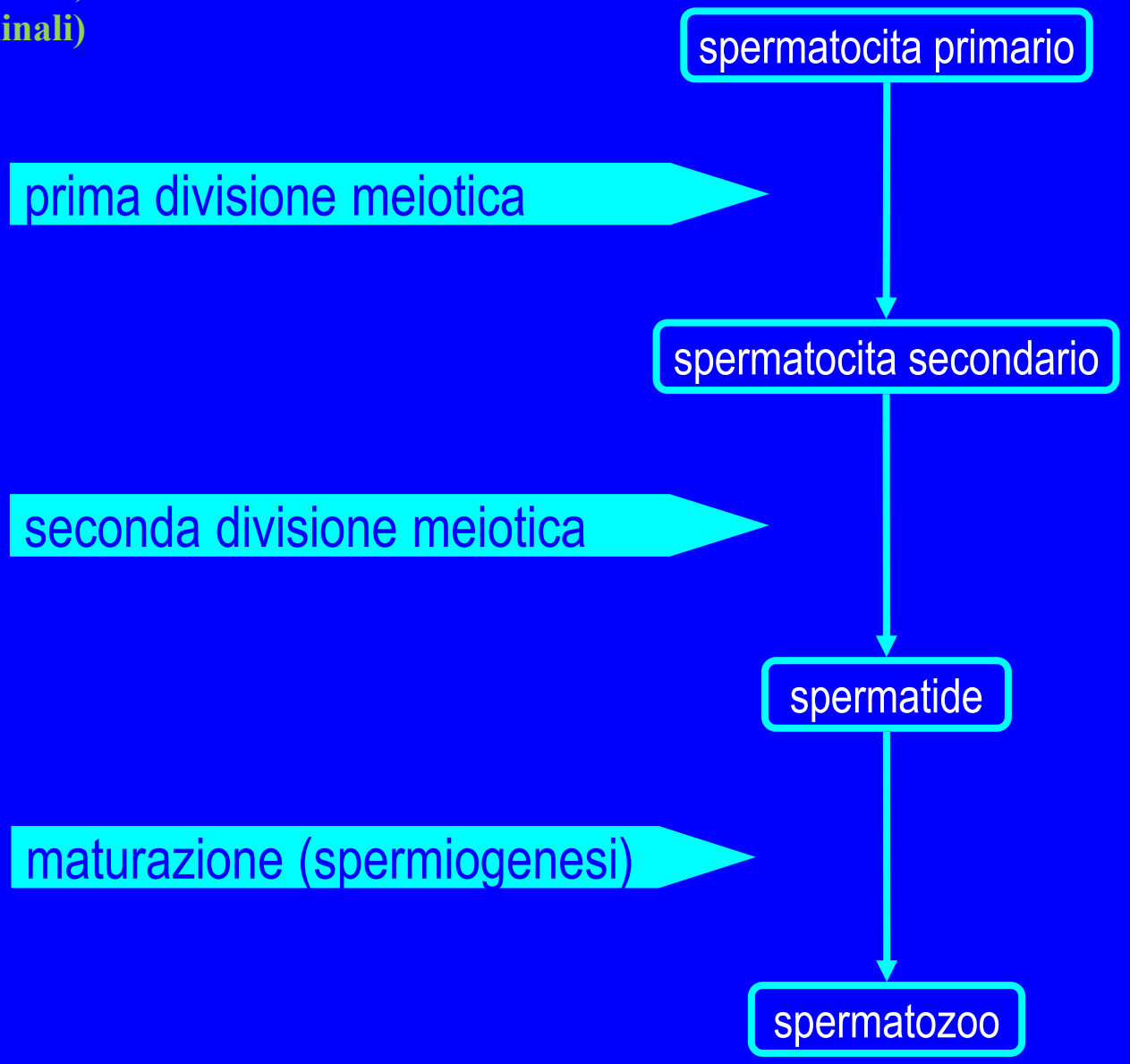
spermatociti primari

duplicazione DNA;
ingresso in leptotene
(inizio meiosi I)



Esistono due tipi di <u>divisione cellulare</u>:
Mitosi (cellule somatiche)
Meiosi (cellule germinali)

spermatogenesi 2



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Mitosi (cellule somatiche)
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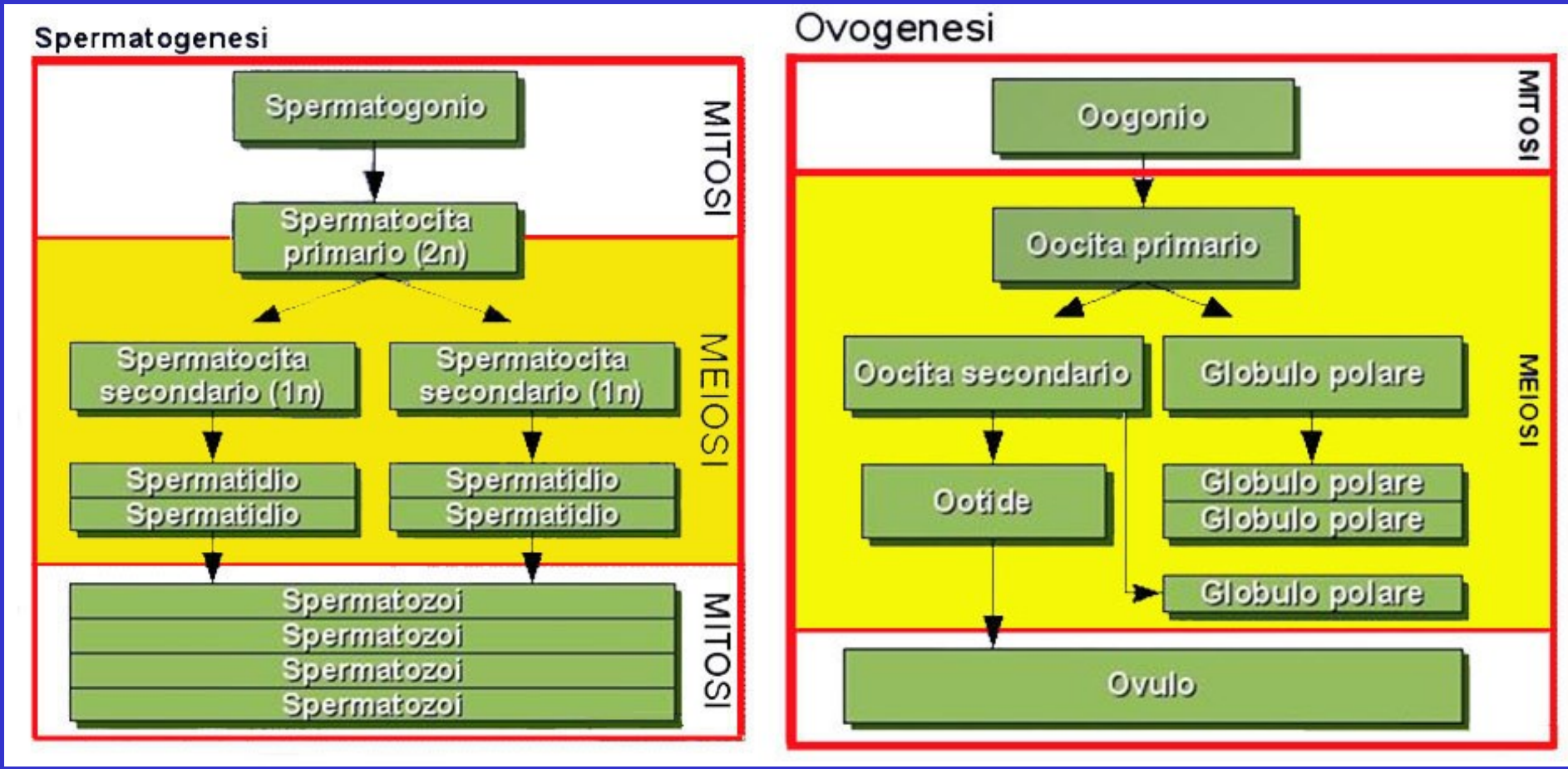


SPERMATOGENESI vs OOGENESI

Meiosi rapida e continua **Meiosi lenta ed a tappe**

Spermatogenesi

E' suddivisa in 3 fasi

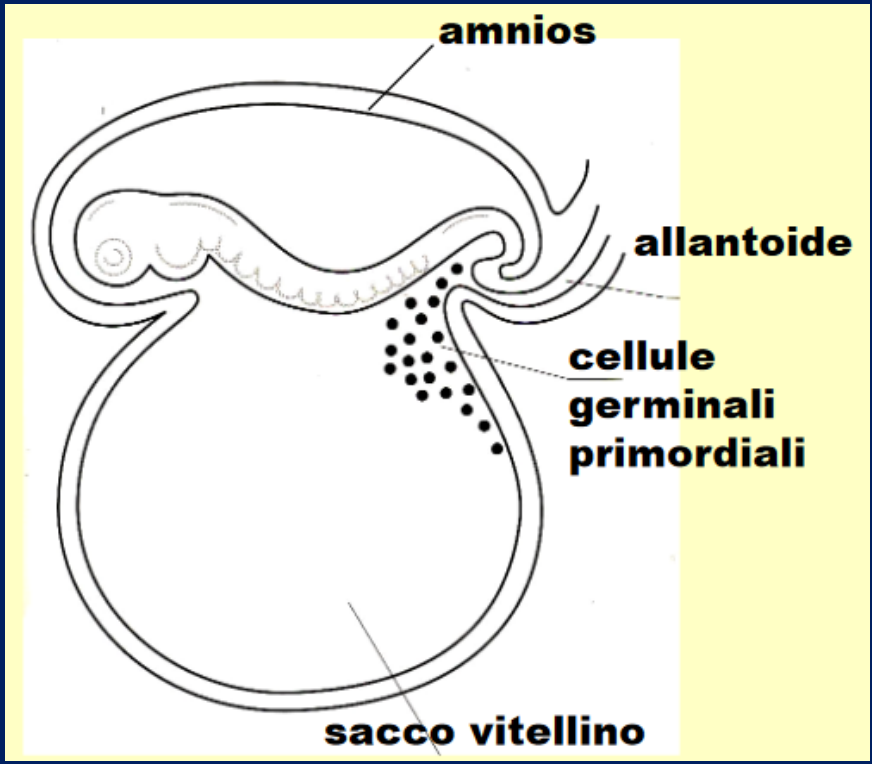
PROLIFERAZIONE	16 giorni
MEIOSI	24 giorni
SPERMIOGENESI	24 giorni
	64 giorni TOT

Durata costante caratteristica per ogni specie

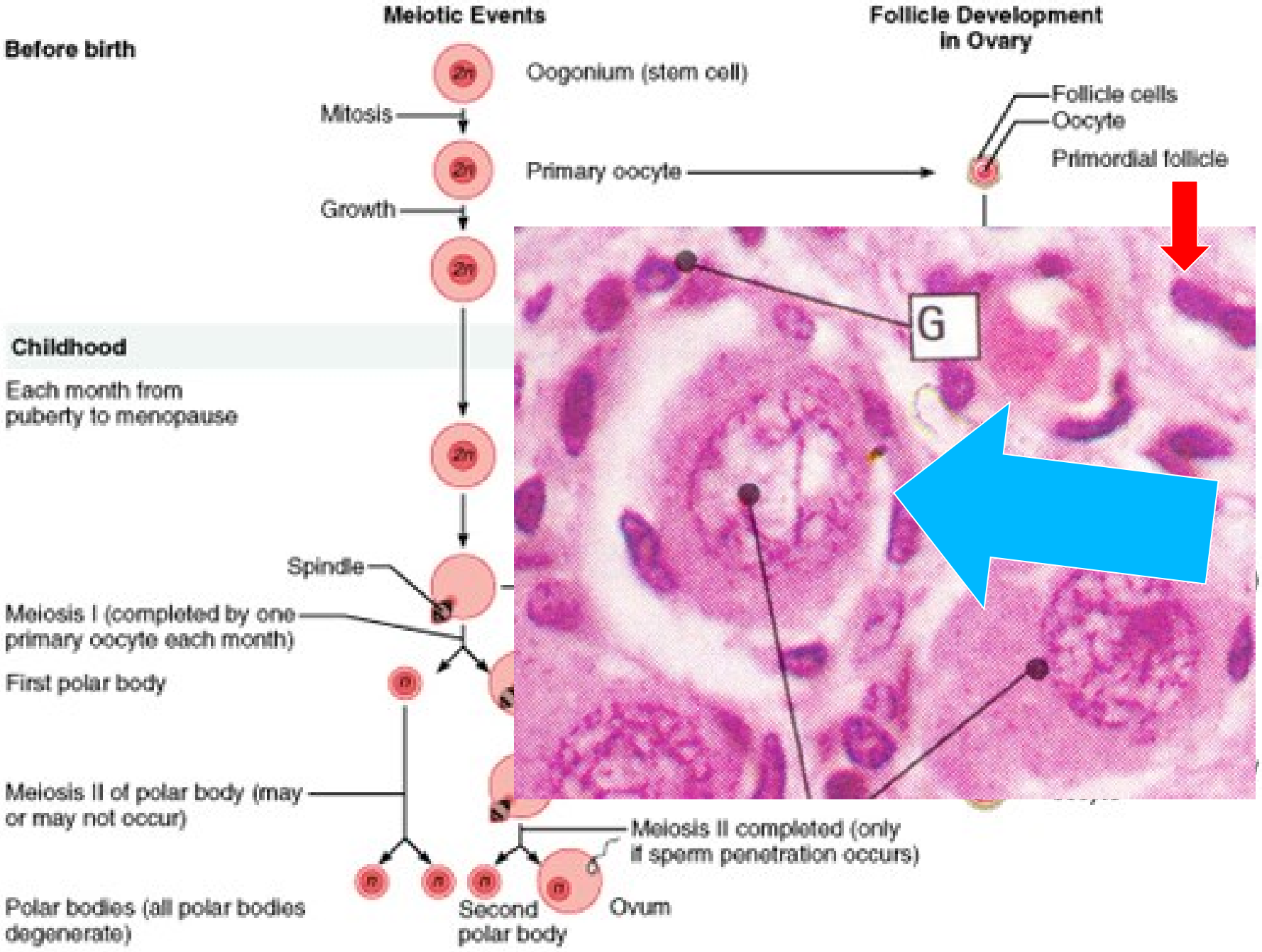
Gametogenesi: cellule germinali

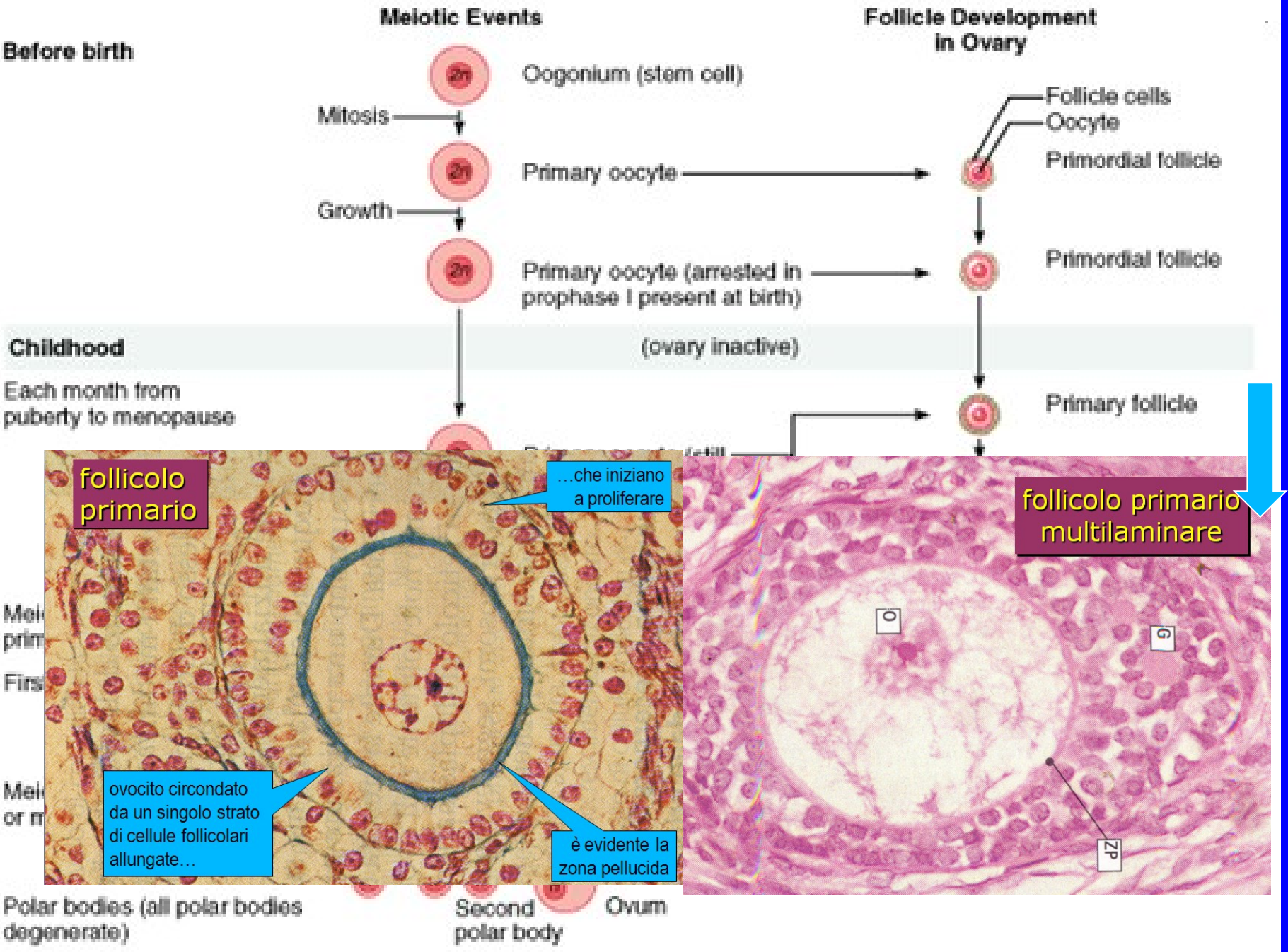
Originano nell' EPIBLASTO (II sett.di sviluppo)

Poi migrano nel sacco vitellino al di fuori dell'embrione



4° sett >>>
MIGRAZIONE
delle CELLULE GERMINALI
in abbozzi gonadi:
Mitosi
Creste genitali


Meiotic Events
Follicle Development in Ovary
Before birth
2n
Oogonium (stem cell)
Mitosis
Primary oocyte
Follicle cells
Oocyte
Primordial follicle
Growth
G
Childhood
Each month from puberty to menopause
Spindle
Meiosis I (completed by one primary oocyte each month)
First polar body
Meiosis II of polar body (may or may not occur)
Meiosis II completed (only if sperm penetration occurs)
n
Polar bodies (all polar bodies degenerate)
Second polar body
Ovum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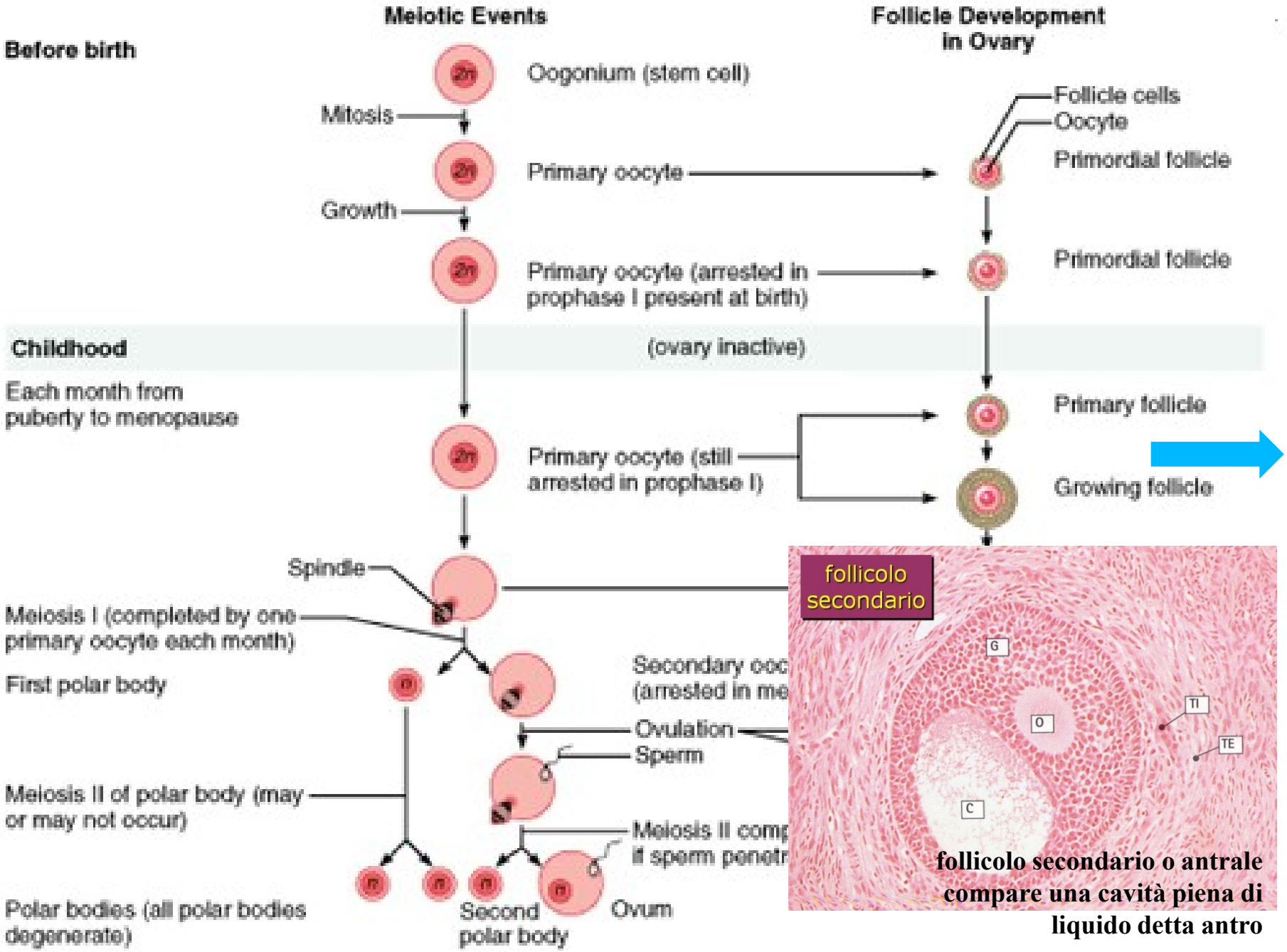
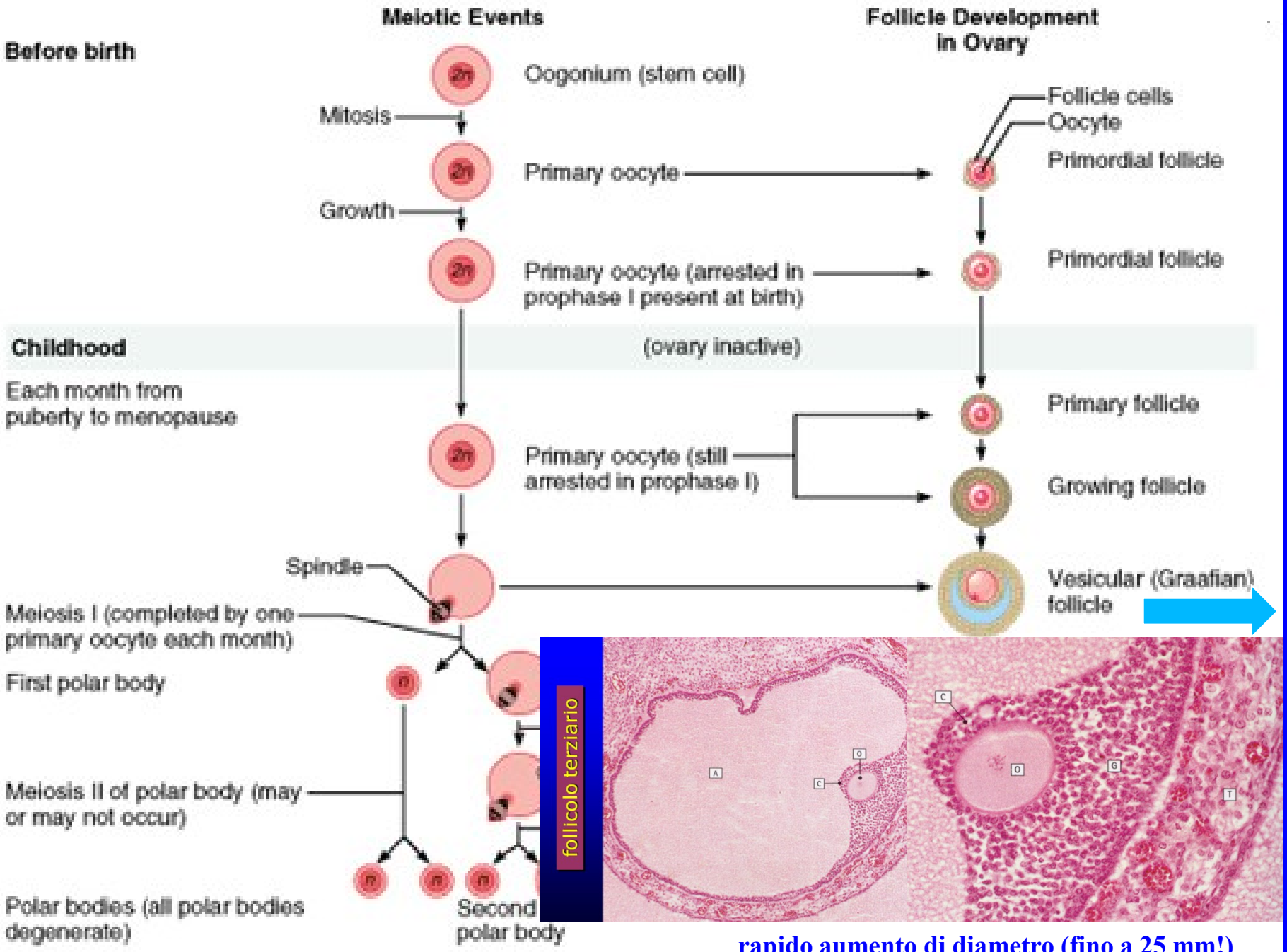
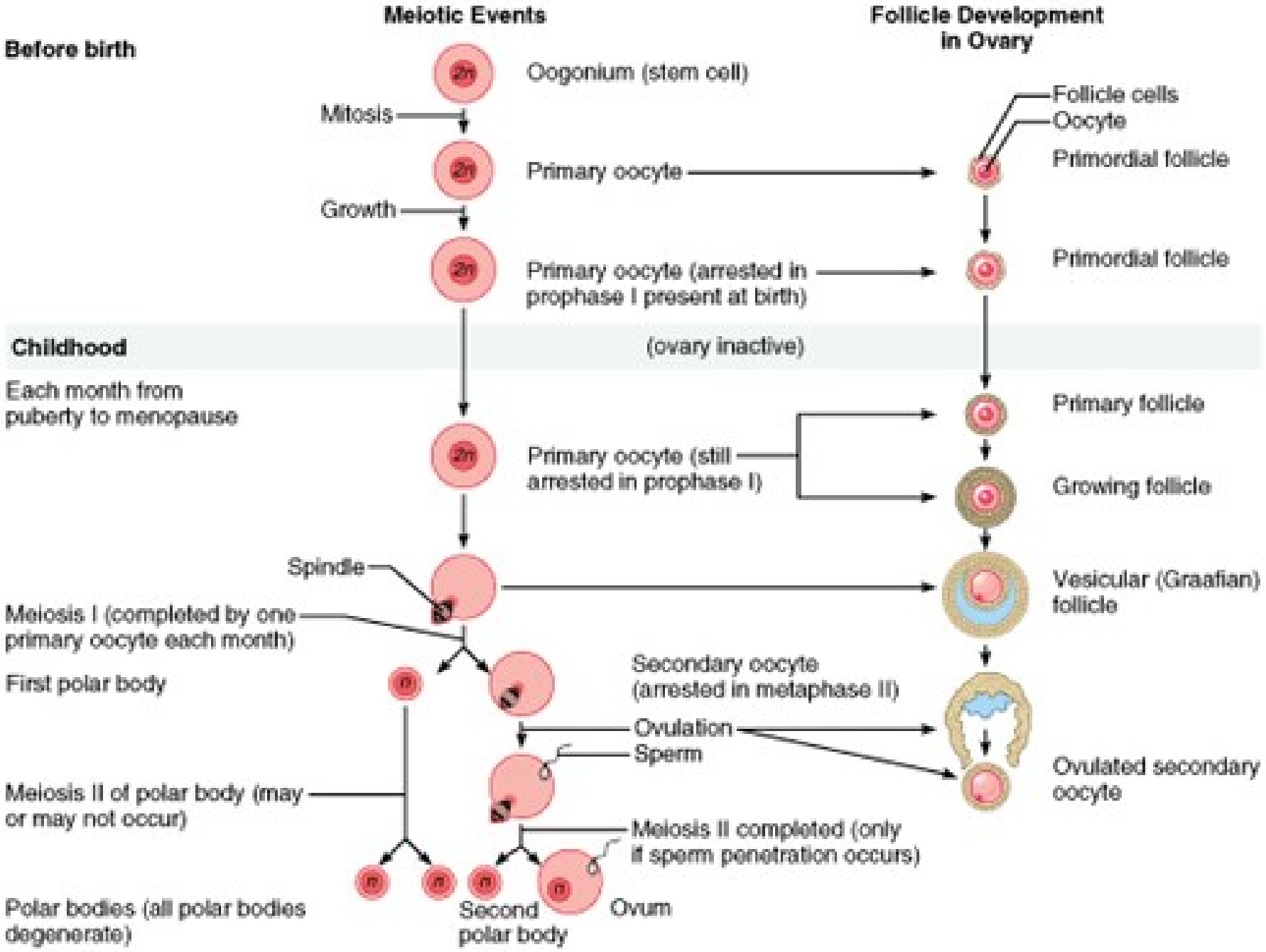
Before birth
2n
Oogonium (stem cell)
Mitosis
Follicle cells
Oocyte
Primordial follicle
Primary oocyte
Growth
Primordial follicle
Primary oocyte (arrested in prophase I present at birth)
Childhood
(ovary inactive)
Each month from puberty to menopause
Primary follicle
follicolo primario
…che iniziano a proliferare
follicolo primario multilaminare
O
G
ZP
ovocito circondato da un singolo strato di cellule follicolari allungate…
è evidente la zona pellucida
Polar bodies (all polar bodies degenerate)
Second polar body
Ovum



follicolo secondario o antrale compare una cavità piena di liquido detta antro



rapido aumento di diametro (fino a 25 mm!)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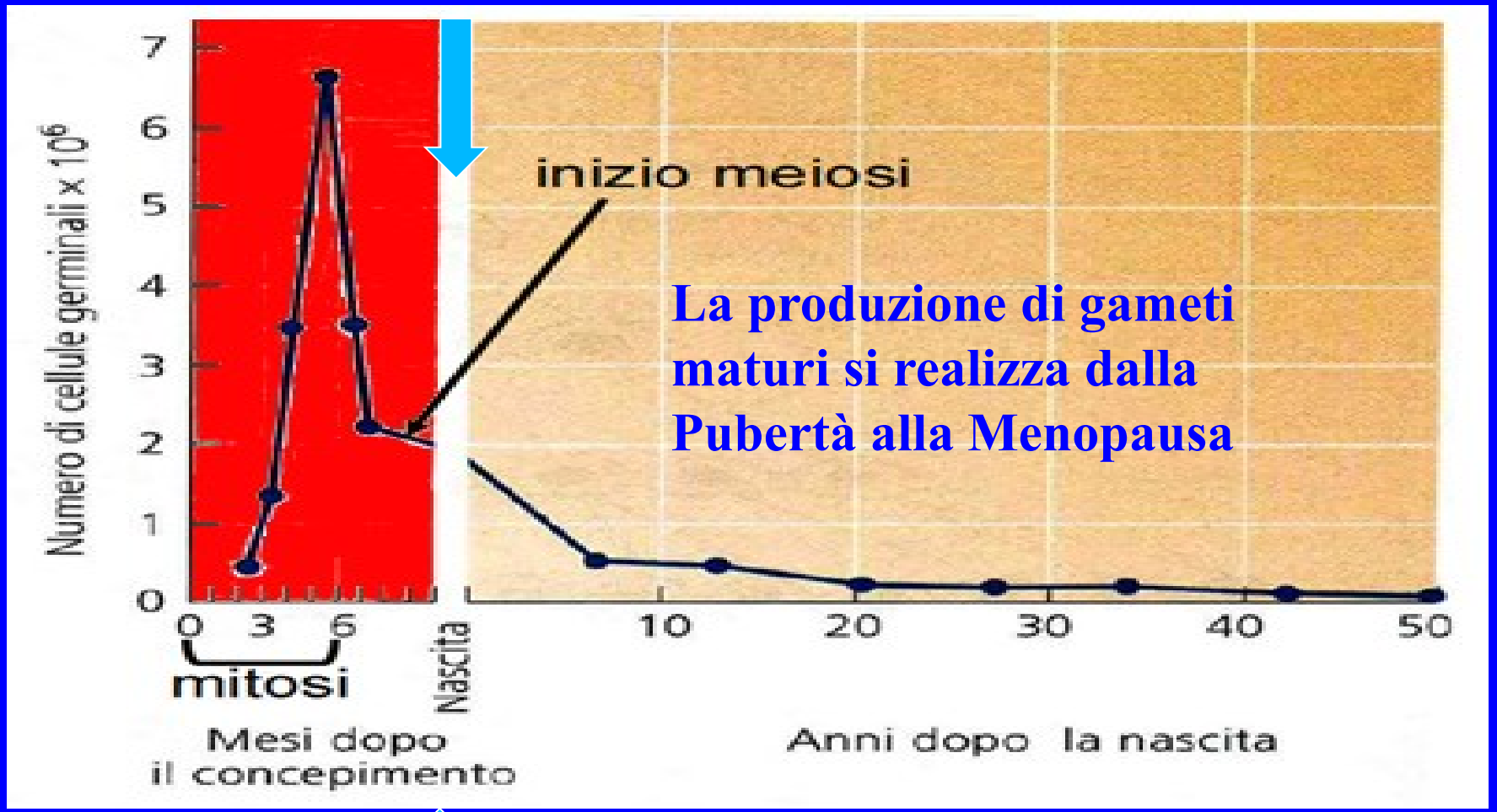
Primordial follicle
Childhood
(ovary inactive)
Each month from puberty to menopause
Primary follicle
Primary oocyte (still arrested in prophase I)
Growing follicle
Spindle
Vesicular (Graafian) follicle
Meiosis I (completed by one primary oocyte each month)
First polar body
n
Secondary oocyte (arrested in metaphase II)
Ovulation
Sperm
Ovulated secondary oocyte
Meiosis II of polar body (may or may not occur)
Meiosis II completed (only if sperm penetration occurs)
Polar bodies (all polar bodies degenerate)
Second polar body
Ovum



Mitosi

(cellule somatiche)

Le cellule figlie, sono identiche alla cellula genitrice

Meiosi

(cellule germinali)

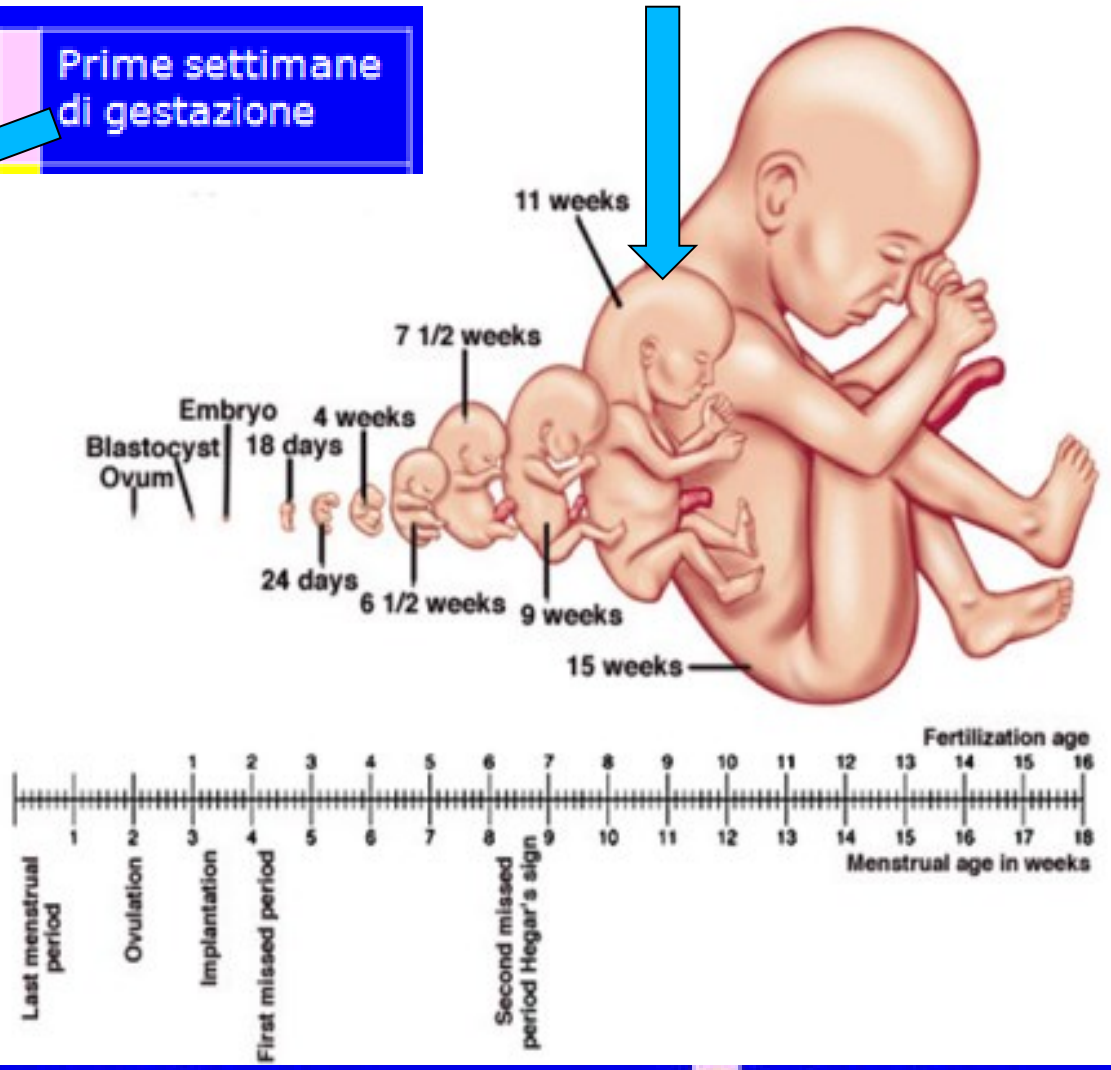
la meiosi genera la diversità genetica

fasi della gametogenesi femminile-1

mitosi degli ovogoni

Prime settimane di gestazione

Dalla **11-12**ª sett. alcuni ovogoni **cessano di proliferare per MITOSI** ed **entrano in MEIOSI, trasformandosi in ovociti primari**



ingresso in leptotene

I Cromosomi diventano visibili come filamenti lunghi e sottili

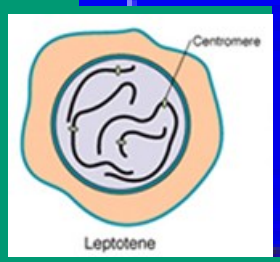
(ovogoni → ovociti primari)

Dal 3° al 7° mese di gestazione

fasi della gametogenesi femminile-1

mitosi degli ovogoni

Prime settimane di gestazione



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(ovogoni → ovociti primari)

Dal 3° al 7° mese di gestazione

ingresso in leptotene

(ovogoni → ovociti primari)

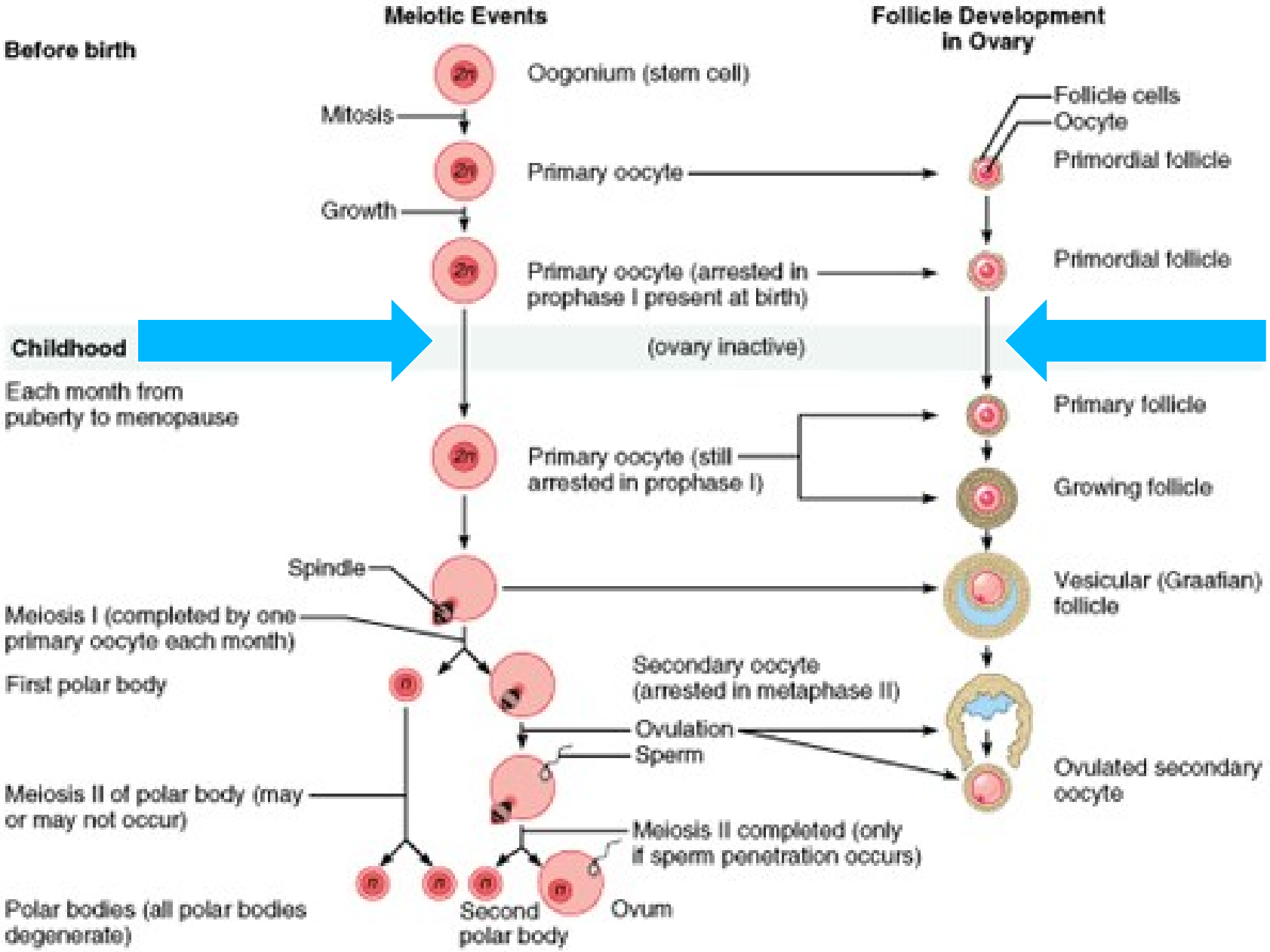
Dal 3° al 7° mese di gestazione

Tutte le cellule germinali sono ovociti primari in meiosi I arrestata in diplotene

Dalle ultime settimane di gestazione alla pubertà

Ovociti primari quiescenti

ENTRO IL 7° MESE DI GESTAZIONE TUTTI GLI OVOGONI SONO DIVENUTI OVOCITI PRIMARI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Sperm
Ovulated secondary oocyte
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Meiosis II completed (only if sperm penetration occurs)
Polar bodies (all polar bodies degenerate)
Second polar body
Ovum

Gametogenesi nei due sessi

- nella femmina:
  - la meiosi inizia in tutte le cellule germinali durante la fase fetale e si arresta prima della nascita
  - la meiosi riprende con la pubertà interessando un solo ovocito per ogni ciclo mestruale
- nel maschio:
  - non si verifica meiosi né durante lo sviluppo prenatale né prima della pubertà
  - con la pubertà inizia la meiosi che rimane simultaneamente attiva in molte cellule germinali per tutta la vita

nota bene:

Nell'ovaio > 6-7 x10^6 ovogoni al 5° mese

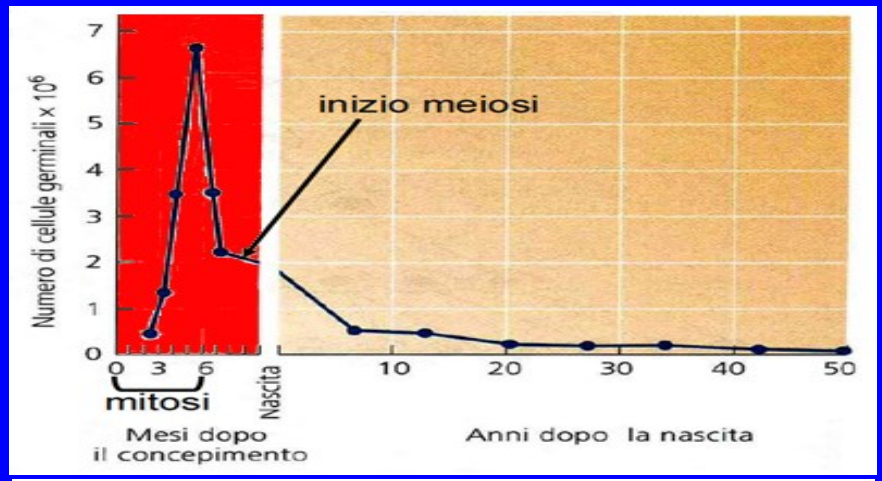
- l'ovaio postnatale

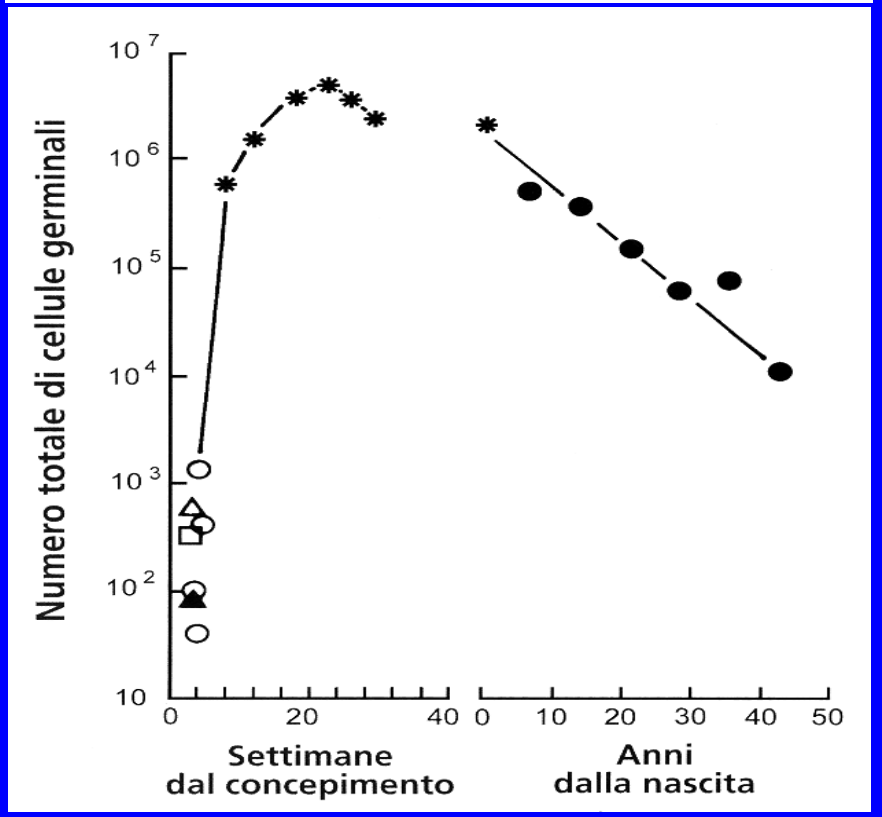
non contiene
cellule germinali
in grado di replicarsi
per mitosi

- alla pubertà una donna

possiede tra 200.000
e 400.000 ovociti
quiescenti

Gametogenesi nei due sessi

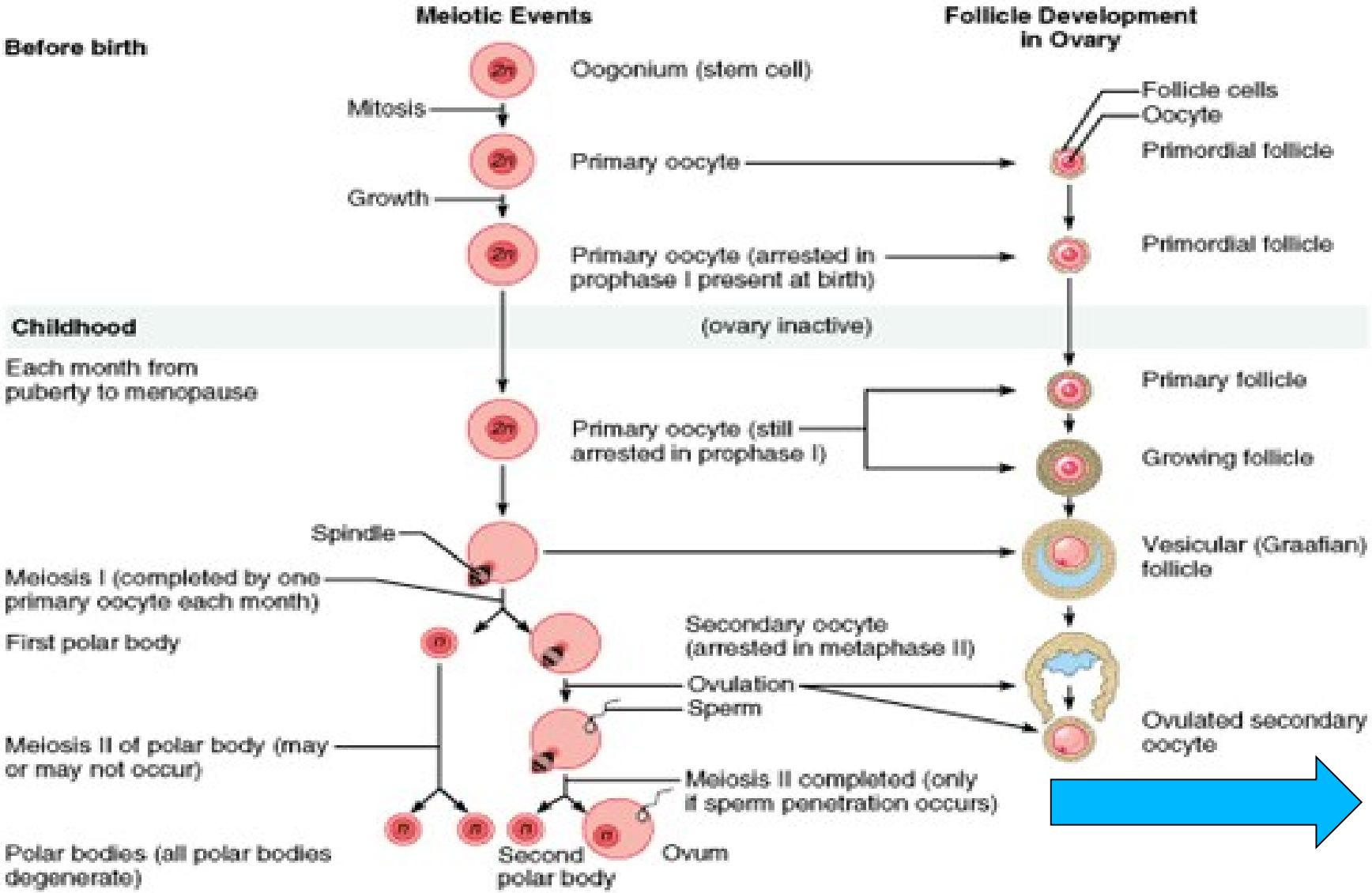




Gametogenesi nei due sessi

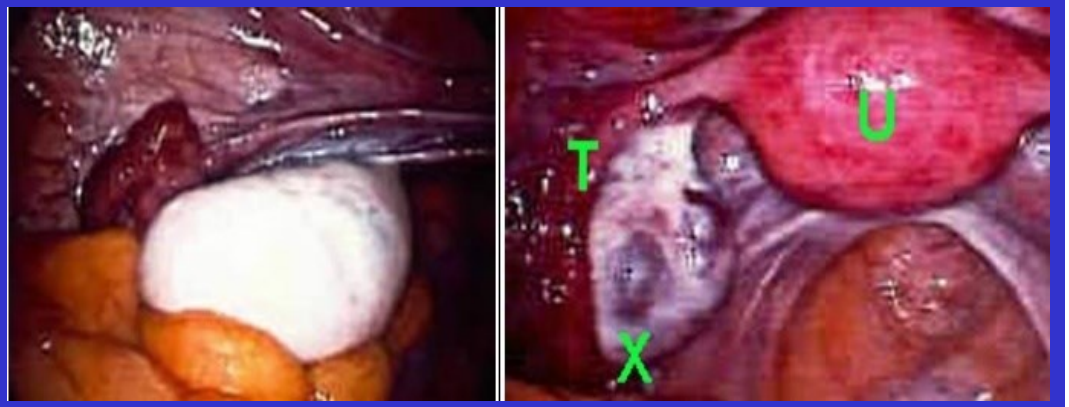
Tutte le fasi della spermatogenesi (proliferazione e maturazione spermatogoni, meiosi alla pubertà)	La proliferazione oogoni, il diff in oociti e la I div meiotica prima nascita
Alla nascita sono presenti spermatogoni elementi staminali	-Alla nascita l'ovaio non ha più ovogoni, ma solo ovociti 1^{ari}
Spermatogenesi: processo continuo	Produzione di cellule uovo: processo ciclico (CICLO OVARICO)
1 Spermatocita I origina 4 spermatozoi	1 Ovocita I origina 1 uovo

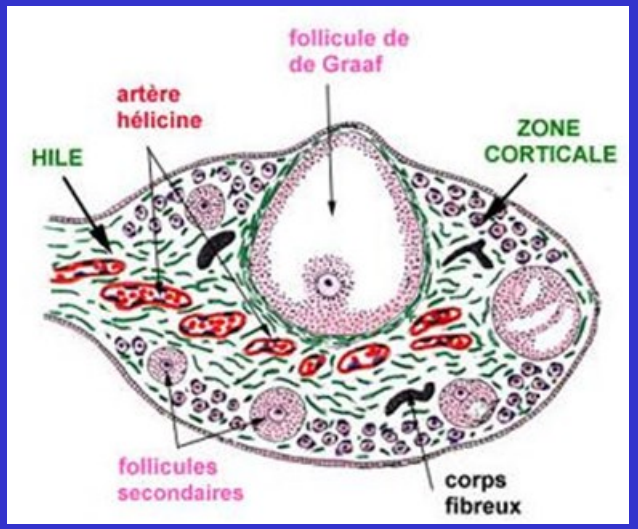
ultime fasi di maturazione



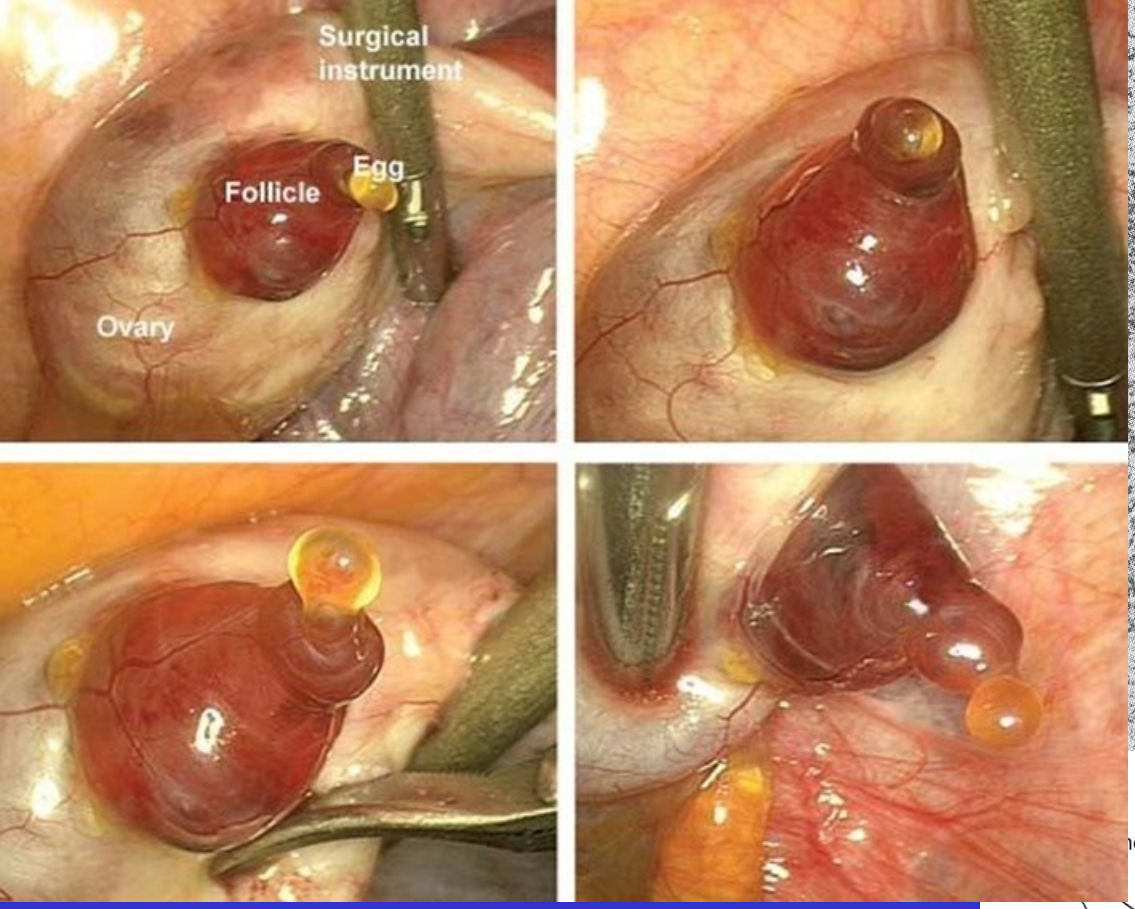
deiescenza del follicolo e ovulazione

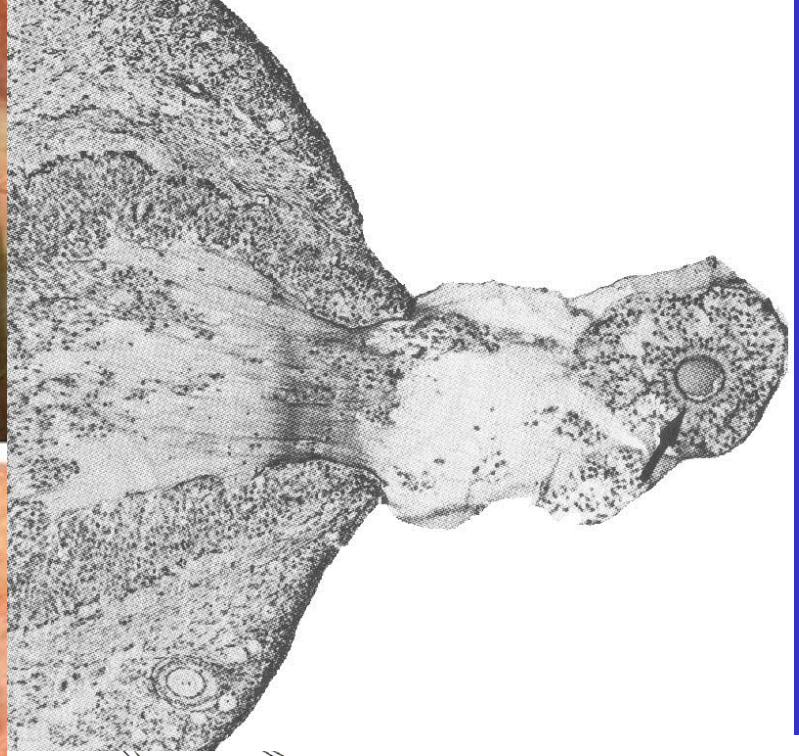
- la parete del follicolo si supericializza: area traslucida (*stigma)*
- lo stigma sporge come una vescichetta sulla superficie dell'ovaio





- **<u>l'ovocita in 10 minuti raggiunge l'ampolla tubarica</u>**
- il **follicolo** che rimane nell'ovaio si trasforma in corpo luteo





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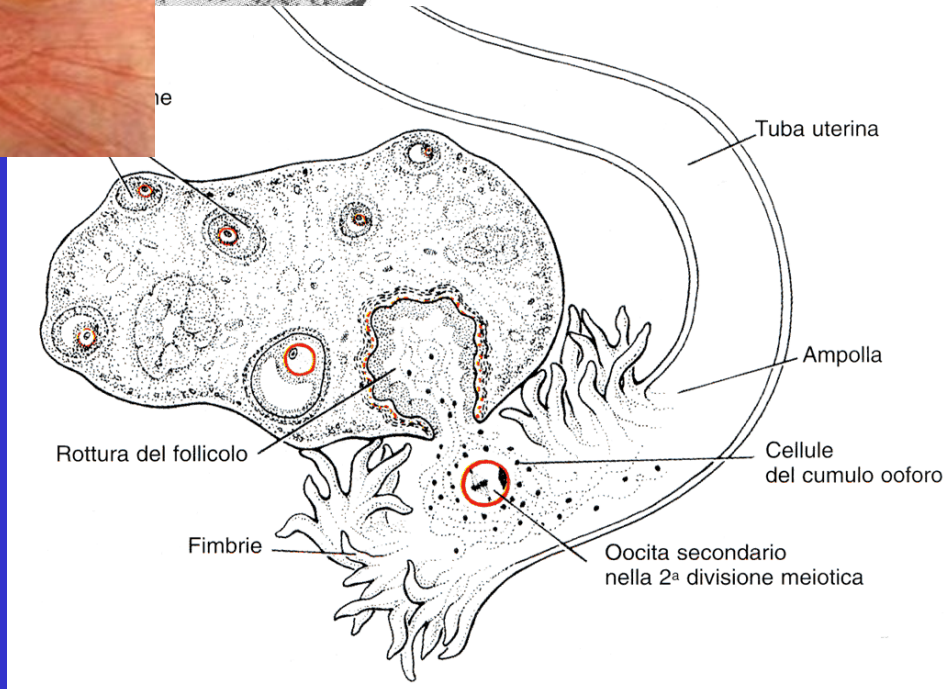
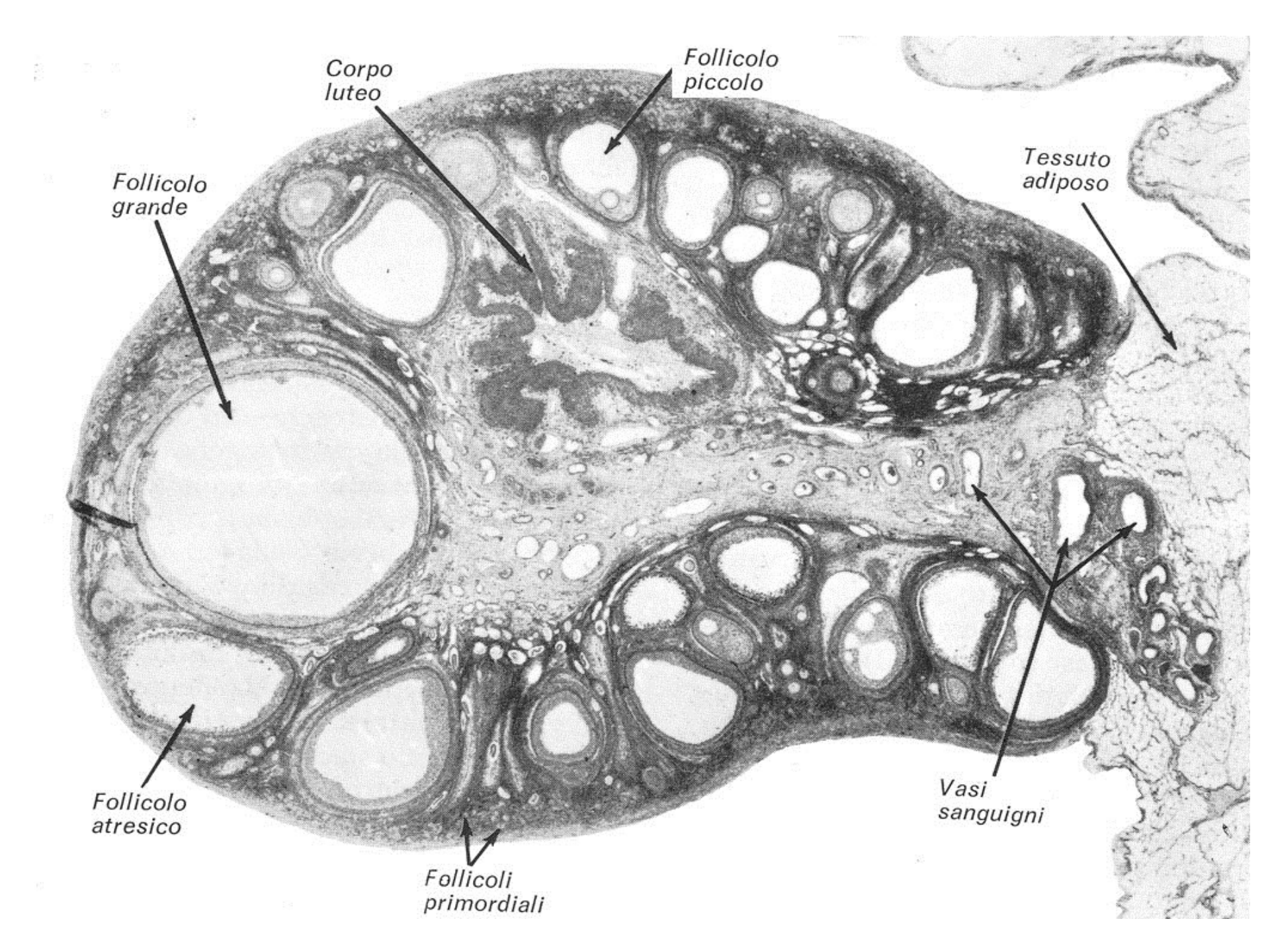
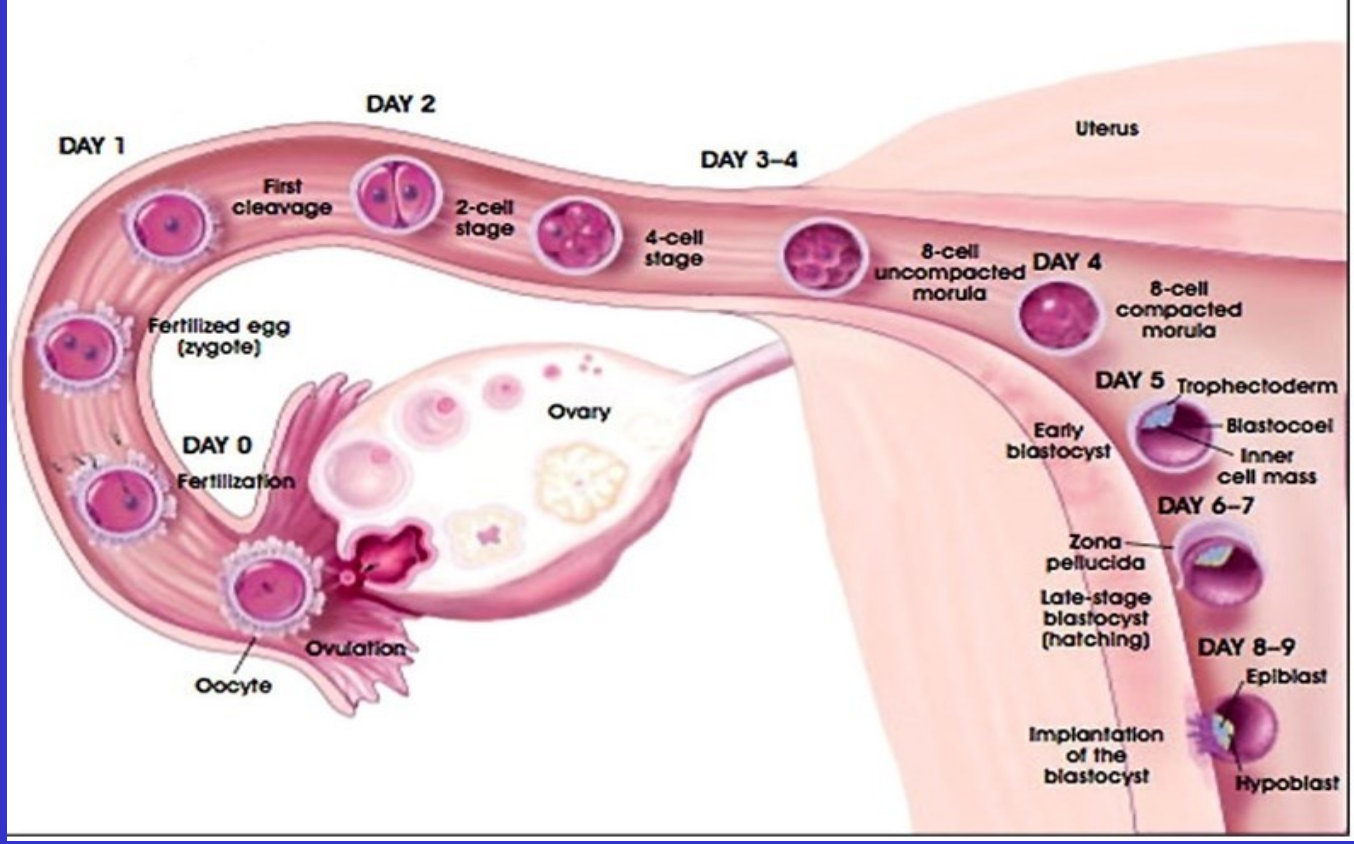
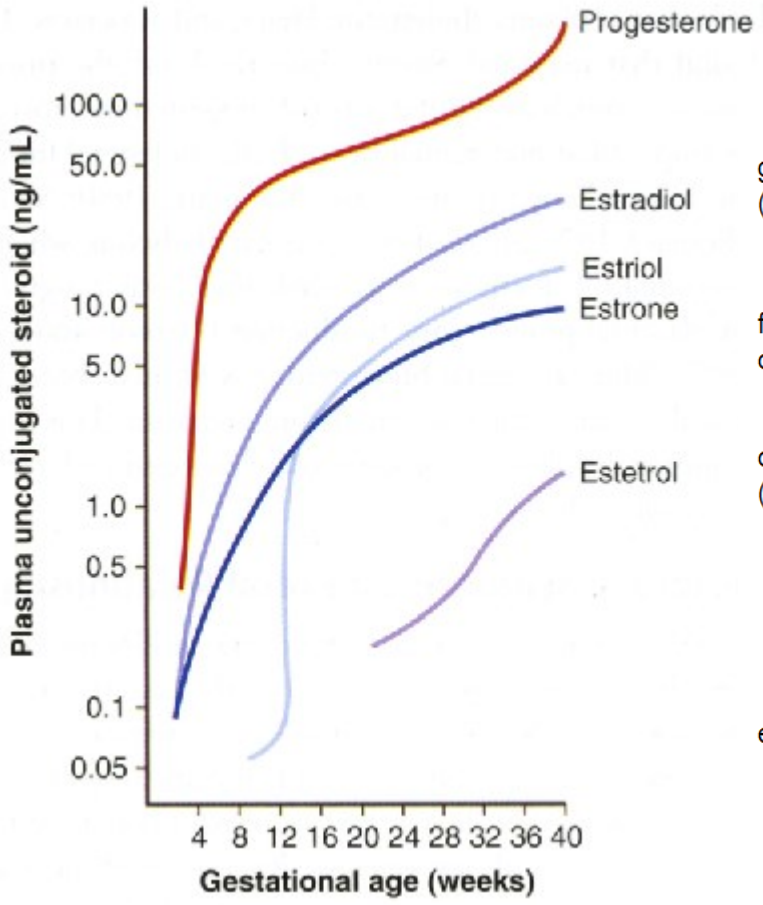



Corpo luteo
Follicolo piccolo
Follicolo grande
Tessuto adiposo
Follicolo atresico
Follicoli primordiali
Vasi sanguigni

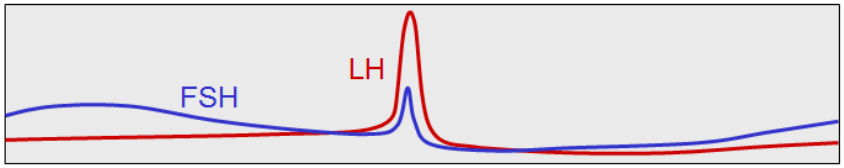
funzione dello spermatozoo



- **ascesa degli spermatozoi fino alla porzione ampollare della tuba uterina**
- **capacitazione degli spermatozoi**
  - rimozione dalla membrana plasmatica acrosomiale di certe componenti proteiche
- **reazione acrosomiale**
  - inizia dopo il legame con la zona pellucida e culmina nel rilascio degli enzimi necessari per penetrare la zona pellucida

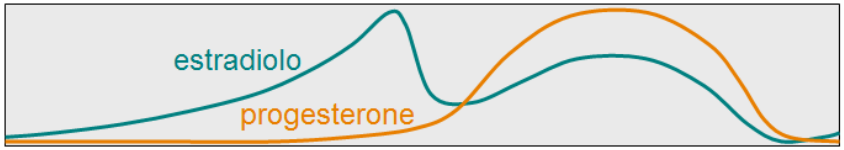


gonadotropine (ormoni ipofisari)

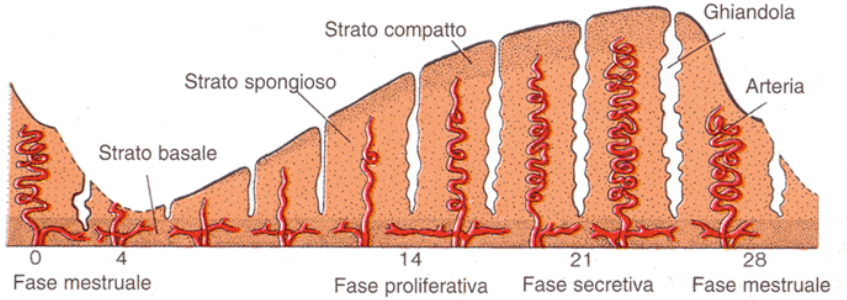


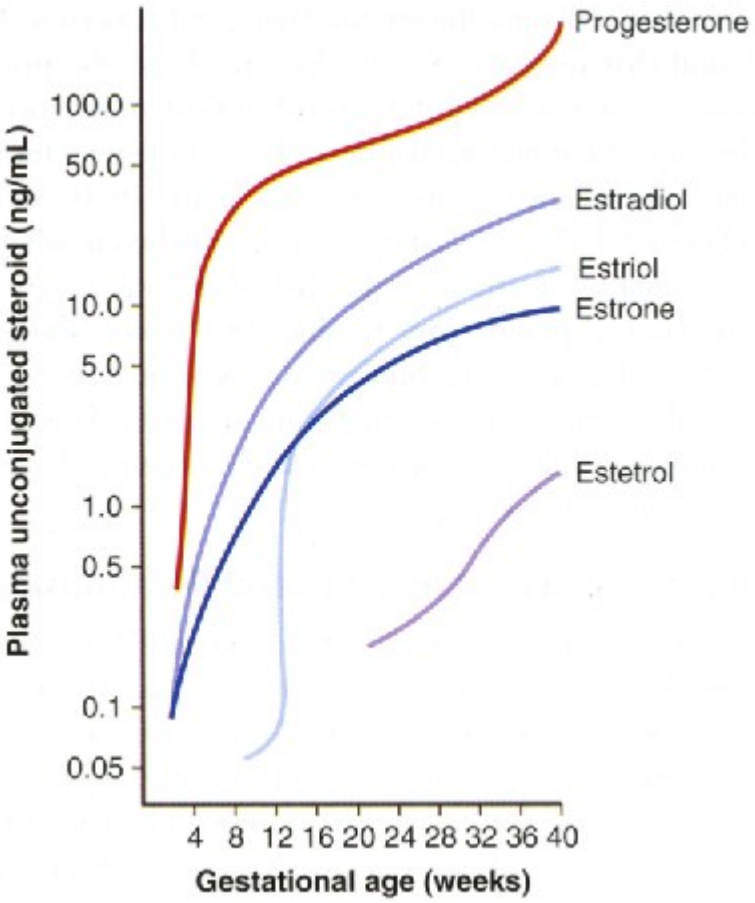
follicolo ovarico

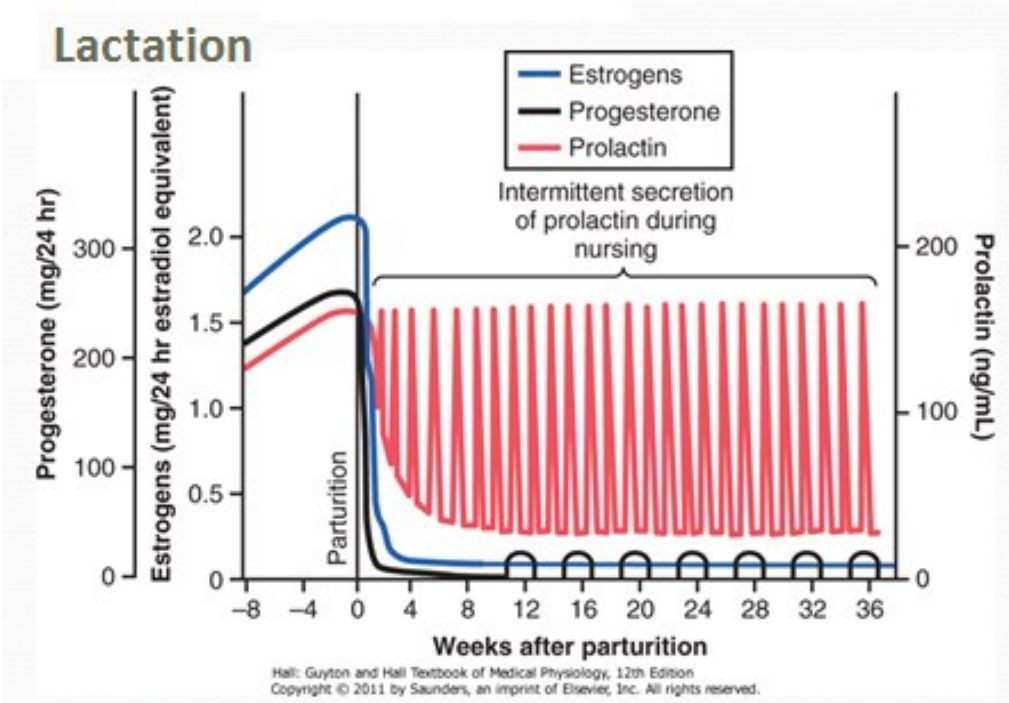
ormoni steroidei (ovarici)



endometrio







Changes in the rates of secretionof estrogens, progesterone, and prolactin for 8 weeks before parturition and 36 weeks thereafter

POOR RESPONDERS

2-30% delle pazienti sottoposte a IVF risultano **POR**
(*Hendriks DJ et al. Fertil Steril 2005)*


Human Reproduction, Vol.26, No.7 pp. 1616–1624, 2011
Advanced Access publication on April 19, 2011 doi:10.1093/humrep/der092

human reproduction

ESHRE PAGES

ESHRE consensus on the definition of 'poor response' to ovarian stimulation for *in vitro* fertilization: the Bologna criteria†

A.P. Ferraretti[1,*], A. La Marca[2], B.C.J.M. Fauser[3], B. Tarlatzis[4], G. Nargund[5], and L. Gianaroli[1] on behalf of the ESHRE working group on Poor Ovarian Response Definition‡

ALMENO DUE TRA LE SEGUENTI:

- Età materna avanzata (≥40 anni) o qualsiasi altro fattore di rischio per POR
- Pregressa POR (≤3 ovociti)
- Test di riserva ovarica anormale: AFC <5-7 follicoli o AMH <0.5-1.1 ng/mL

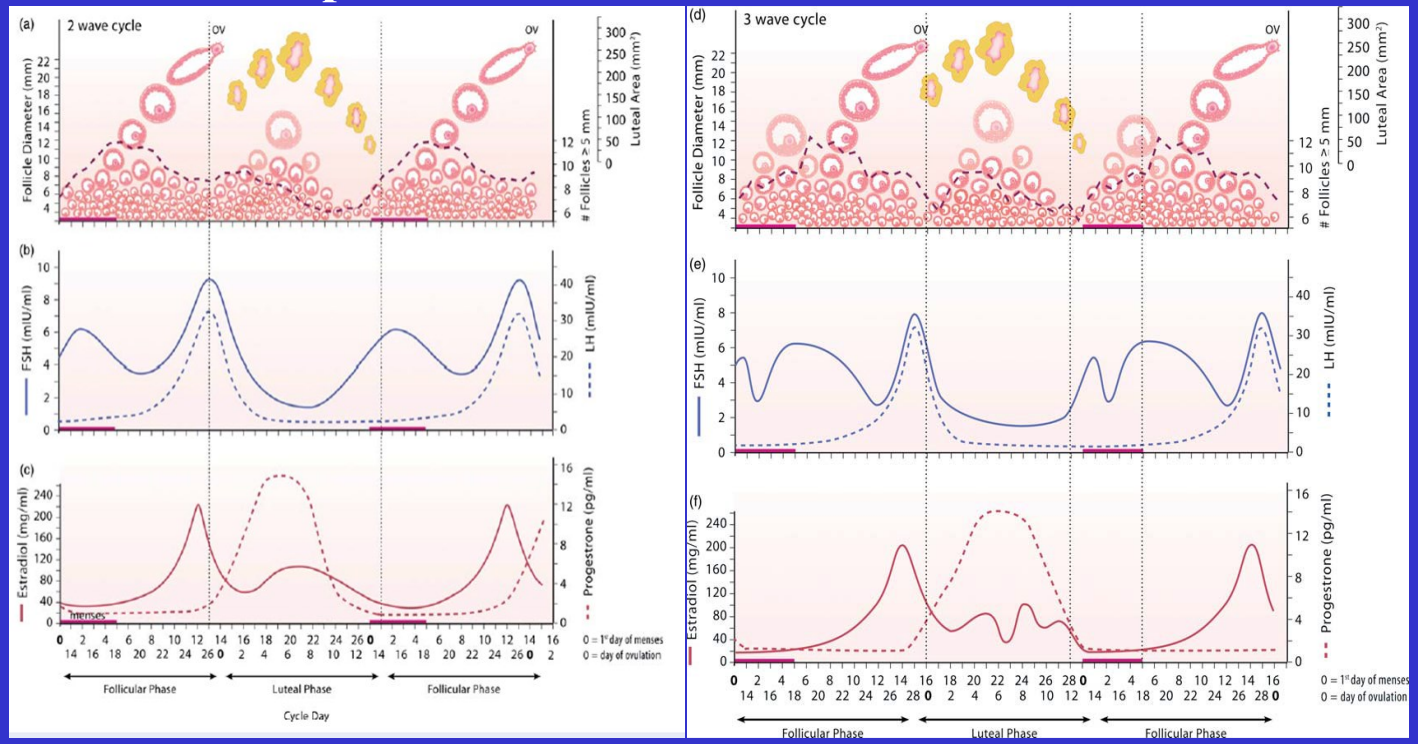
OPPURE

- Due episodi di POR in seguito a stimolazione massima

FOLLICOLOGENESI

Multiple antral follicle waves

Baerwald A et al. HumReprod Update 2012, 18:73-91

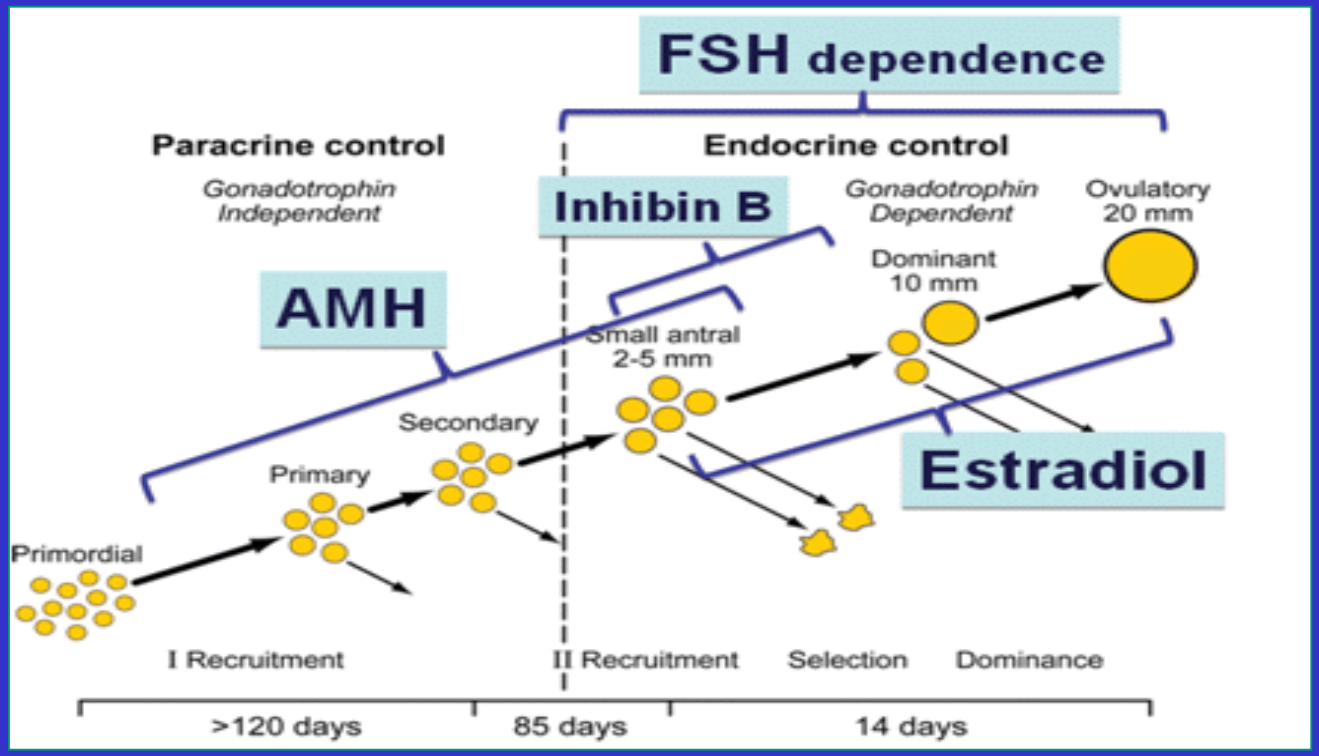


UNA VOLTA si riteneva che il reclutamento follicolare derivasse da una singola l'onda dello sviluppo del follicolo , esclusivamente durante fase follicolare del ciclo.

OGGI è documentato che durante il ciclo sono reclutate 2 o 3 onde suggerendo che la crescita del follicolo antrale puo iniziare in diverse fasi di ciclo. Solo una di queste onde finisce con ovulazione, altre onde sono anovulatorie.

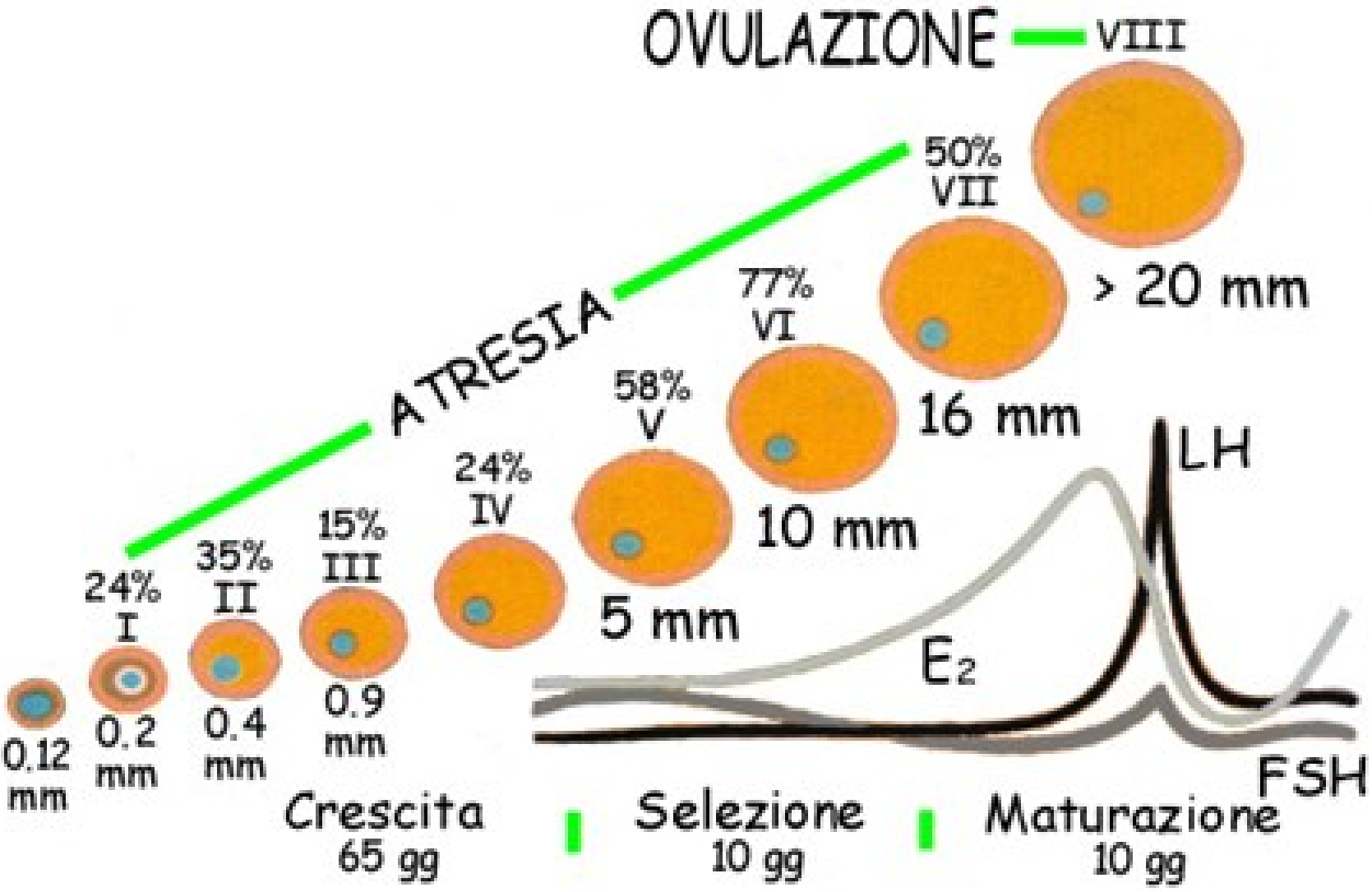
Nelle pazienti poor responder , a causa delle alterazioni nella follicologenesi, spesso troviamo nella conta dei follicoli antrali un pool di follicoli di diverse dimensioni.

FOLLICOLOGENESI

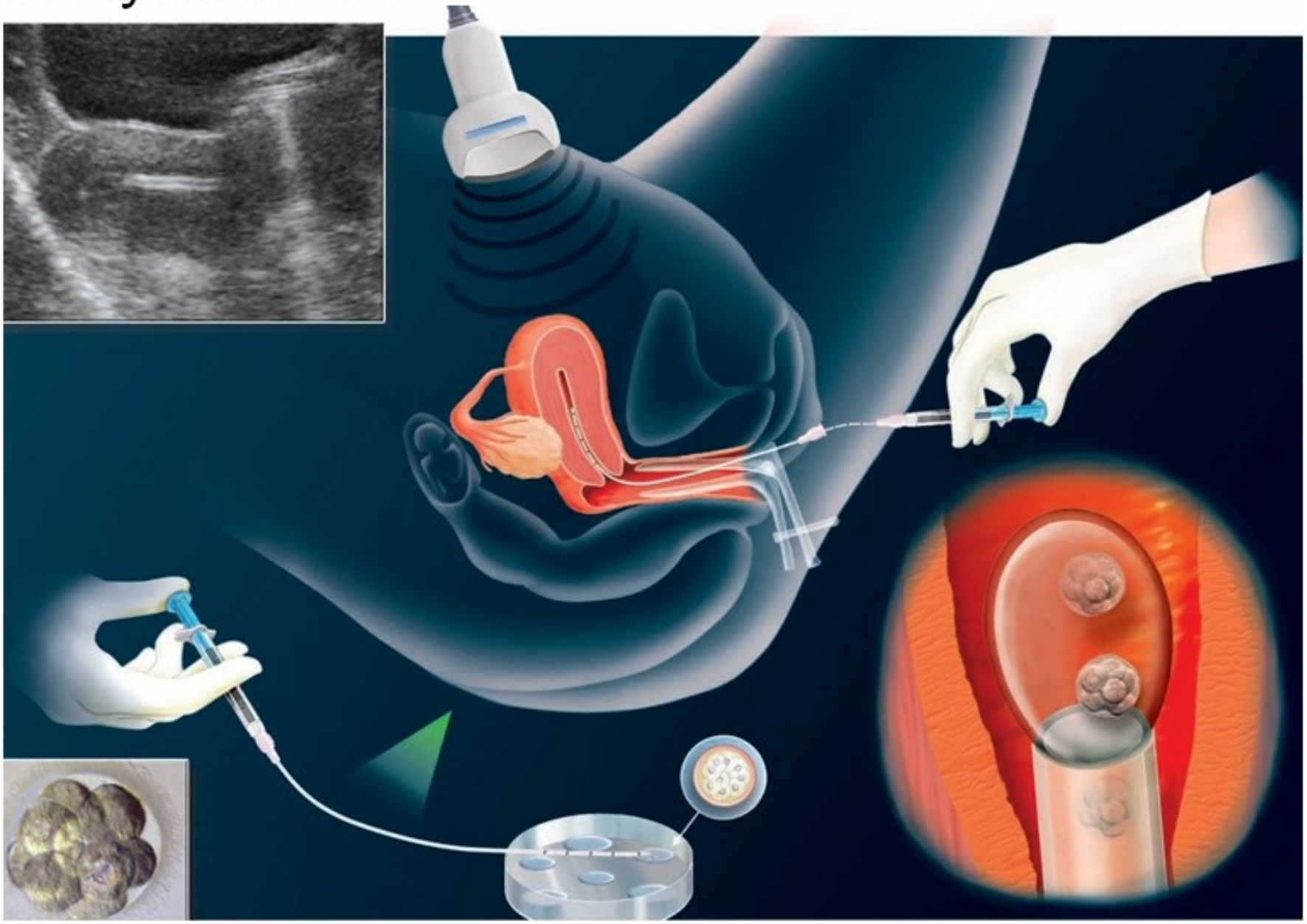


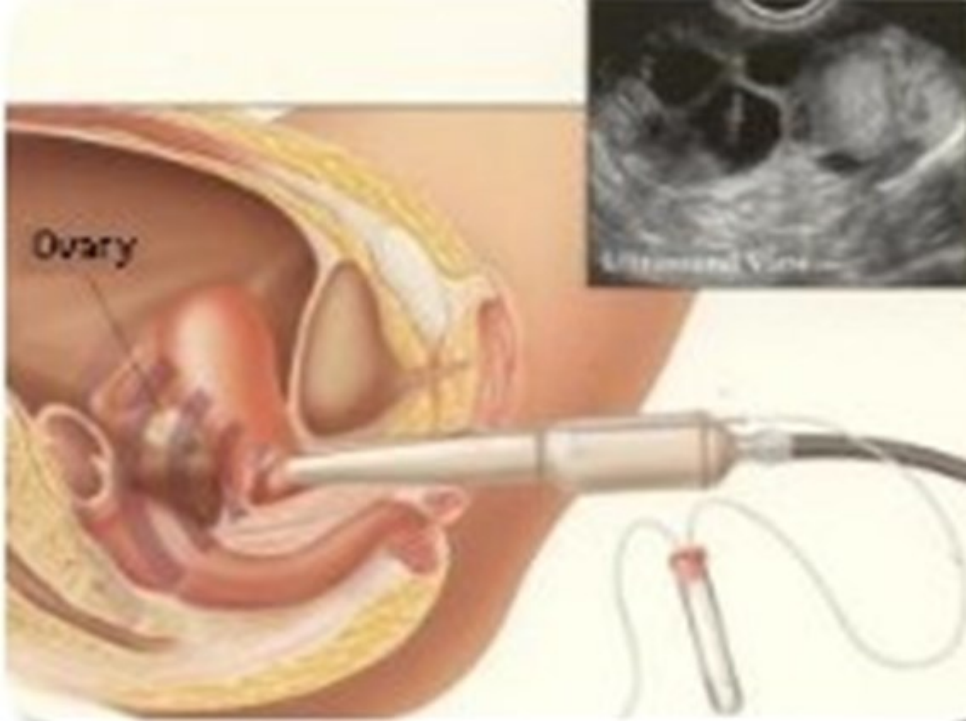
Gougeon et al. Endocrine review 1996;2:121-151.

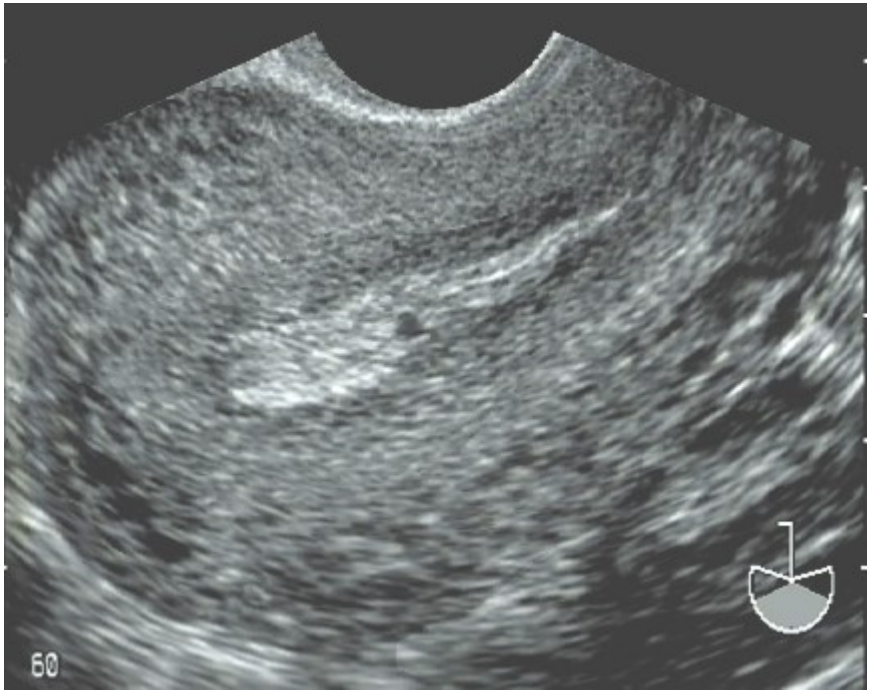
- Dura 290 giorni, all' incirca 10 cicli mestruali.
- **Fase preantrale**: gonadotropino-indipendente, regolazione paracrina e autocrina.
- **Fase antrale**: sviluppo del follicolo contenente l'ovocita sotto controllo delle gonadotropine con la secrezione di androgeni ed estrogeni da parte del follicolo.


OVULAZIONE
VIII
50%
VII
> 20 mm
77%
VI
16 mm
58%
V
10 mm
24%
IV
5 mm
15%
III
0.9 mm
35%
II
0.4 mm
24%
I
0.2 mm
0.12 mm
ATRESIA
LH
E2
FSH
Crescita
65 gg
Selezione
10 gg
Maturazione
10 gg

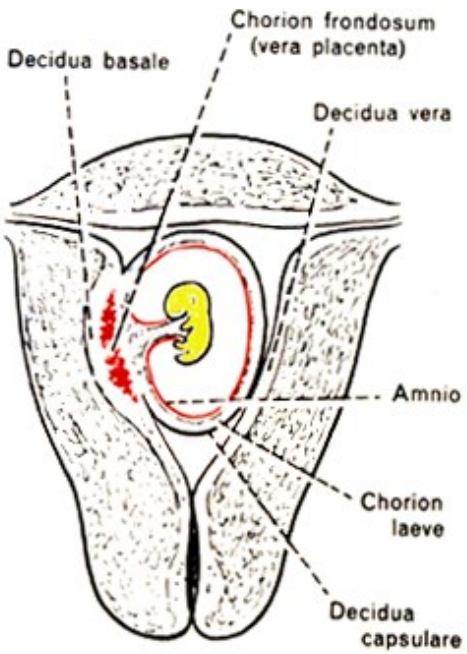
Embryotransfer

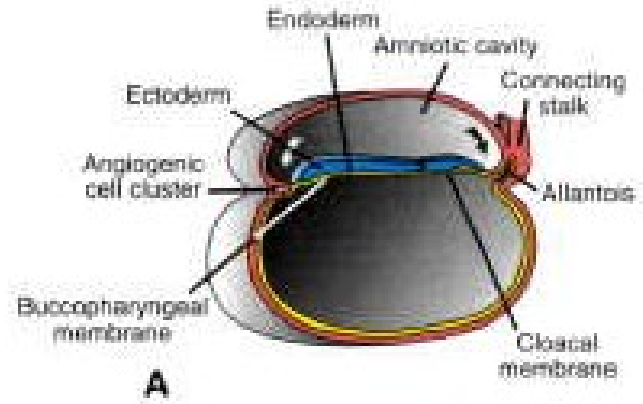


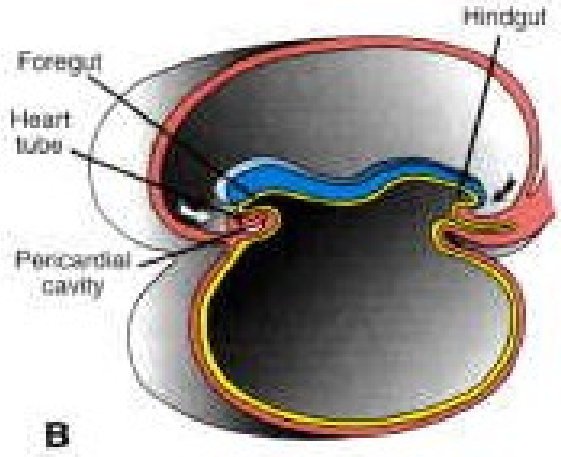

Ovary

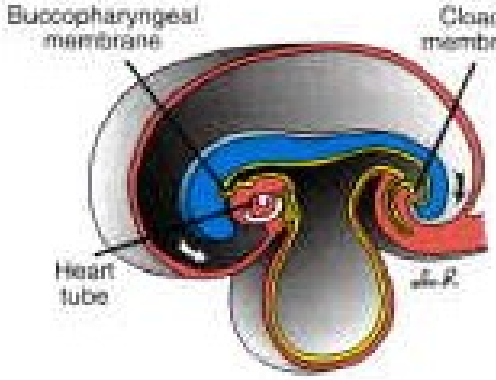

60

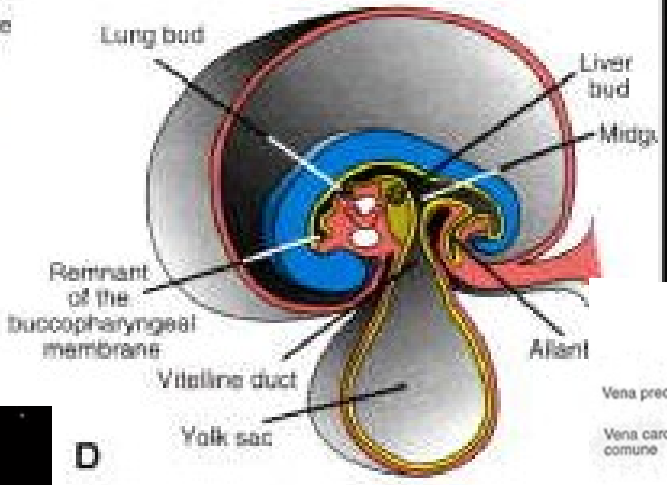

T


Chorion frondosum
(vera placenta)
Decidua basale
Decidua vera
Amnio
Chorion
laeve
Decidua
capsulare

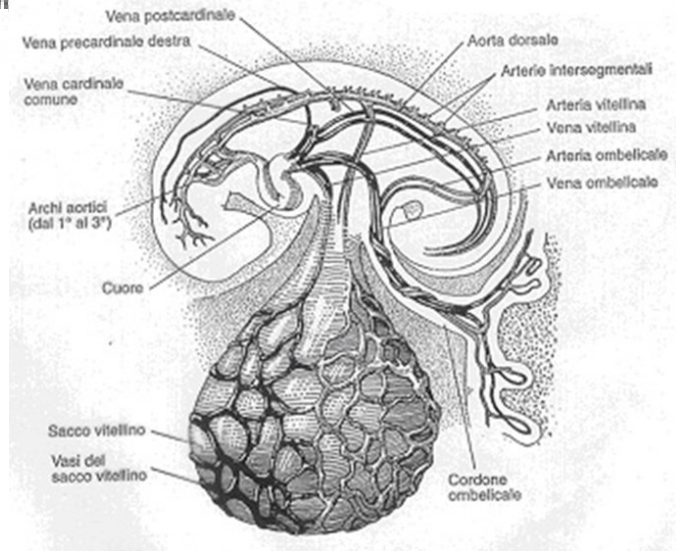


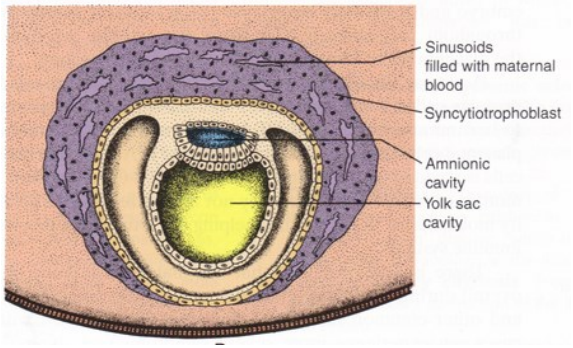


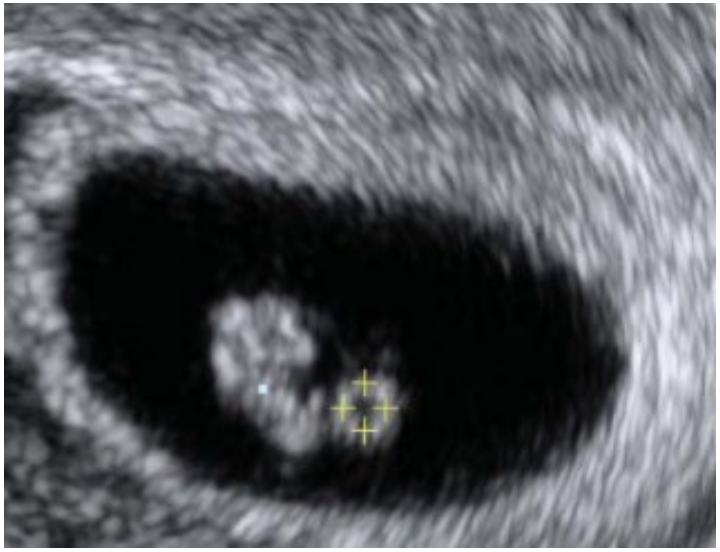


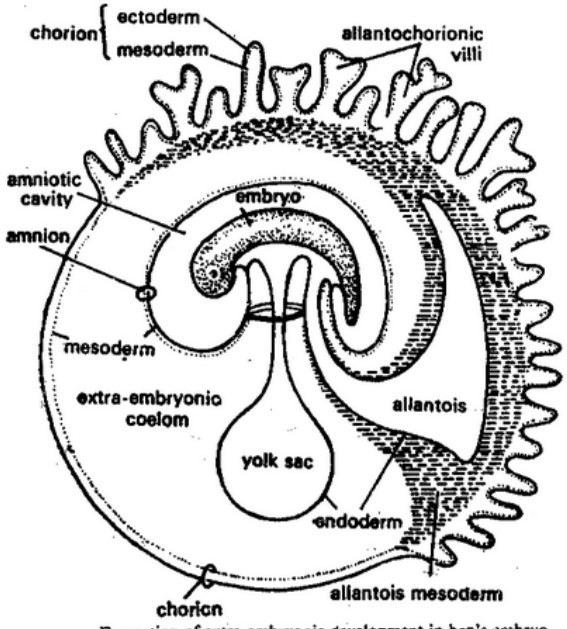


Sviluppo del sistema arterioso

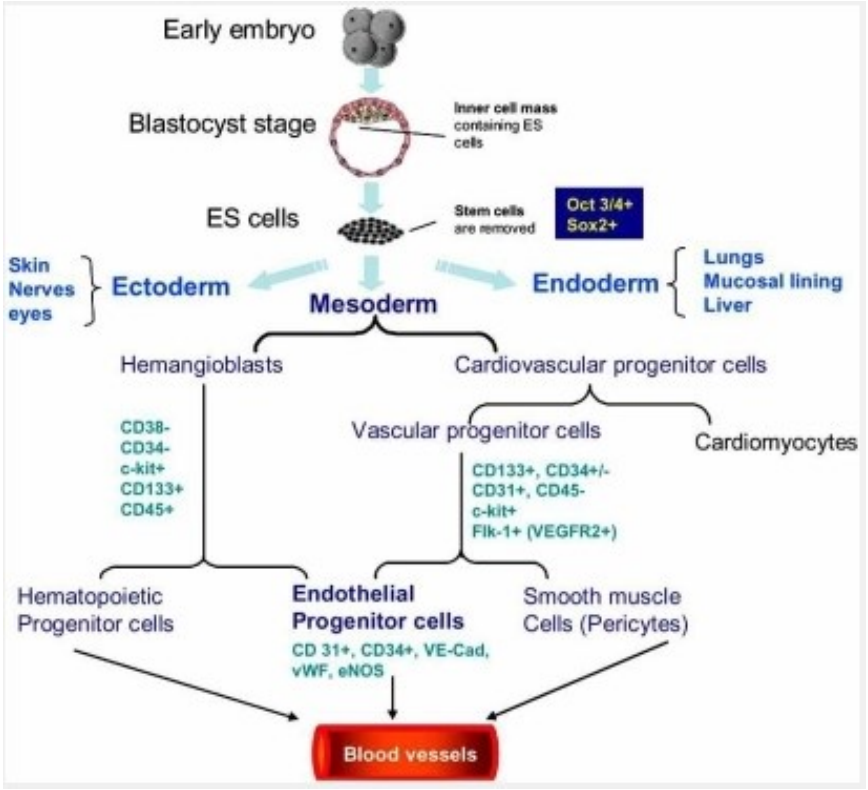


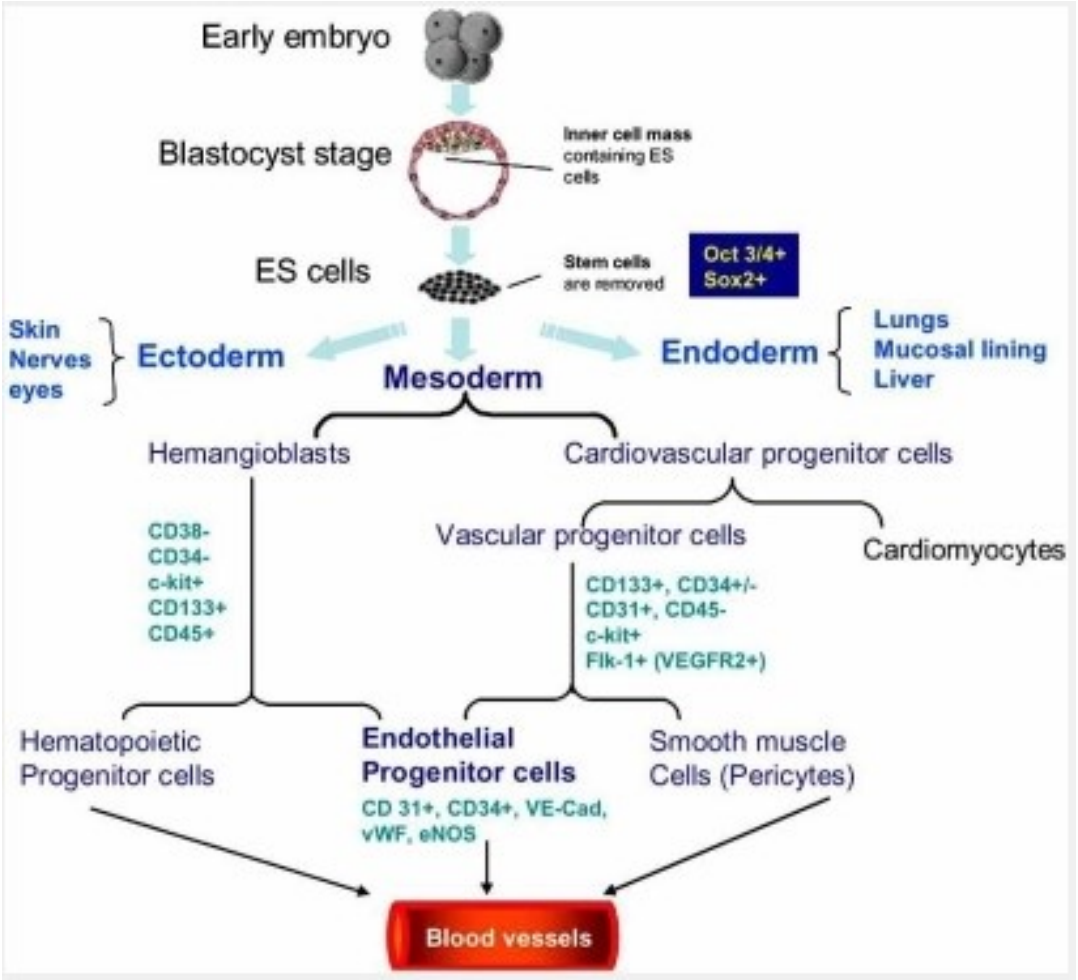






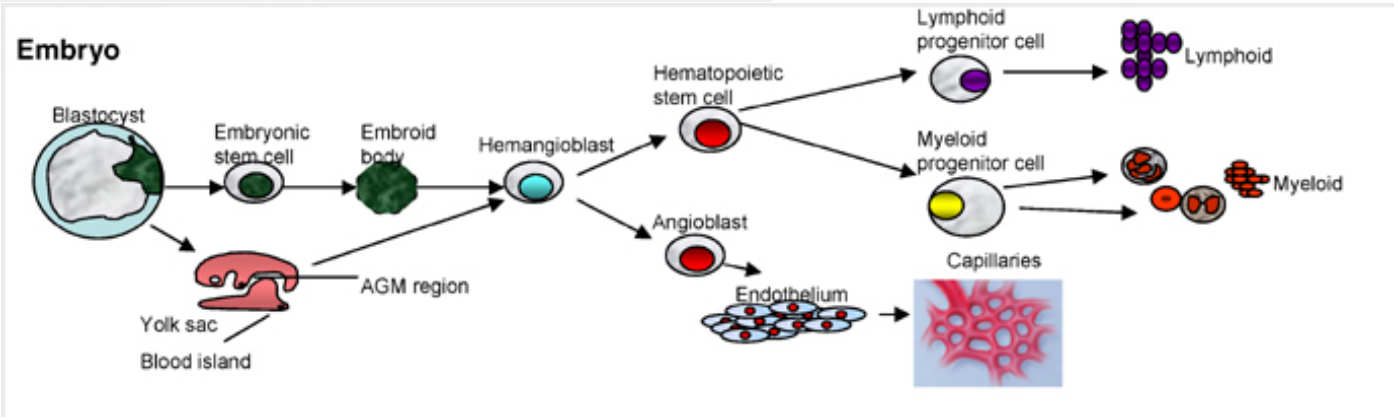
Formation of extra-embryonic development in hen's embryo

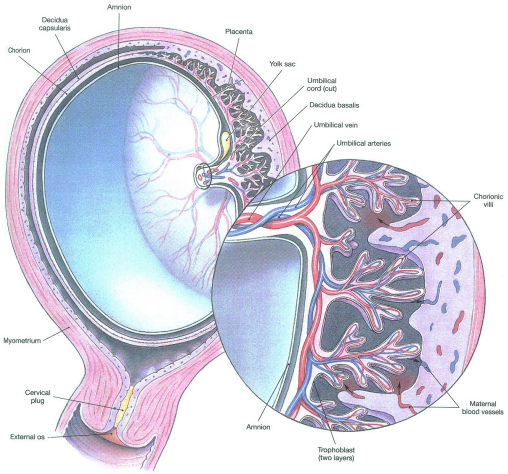



Early embryo
Blastocyst stage
Inner cell mass containing ES cells
ES cells
Stem cells are removed
Oct 3/4+
Sox2+
Skin
Nerves
eyes
Ectoderm
Mesoderm
Endoderm
Lungs
Mucosal lining
Liver
Hemangioblasts
Cardiovascular progenitor cells
CD38-
CD34-
c-kit+
CD133+
CD45+
Vascular progenitor cells
Cardiomyocytes
CD133+, CD34+/-
CD31+, CD45-
c-kit+
Flk-1+ (VEGFR2+)
Hematopoietic Progenitor cells
Endothelial Progenitor cells
CD 31+, CD34+, VE-Cad, vWF, eNOS
Smooth muscle Cells (Pericytes)
Blood vessels

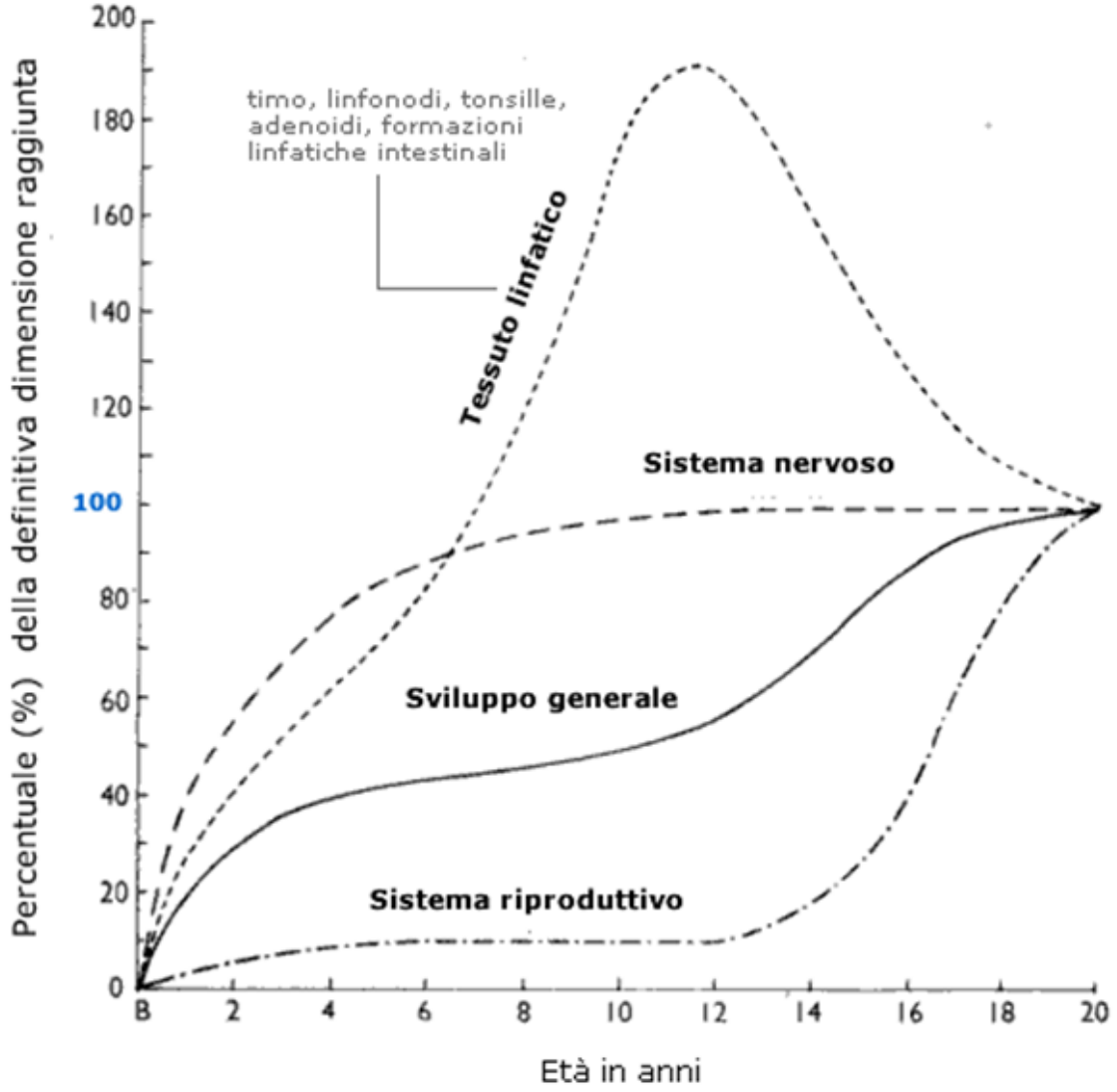

7^3 w
CRL

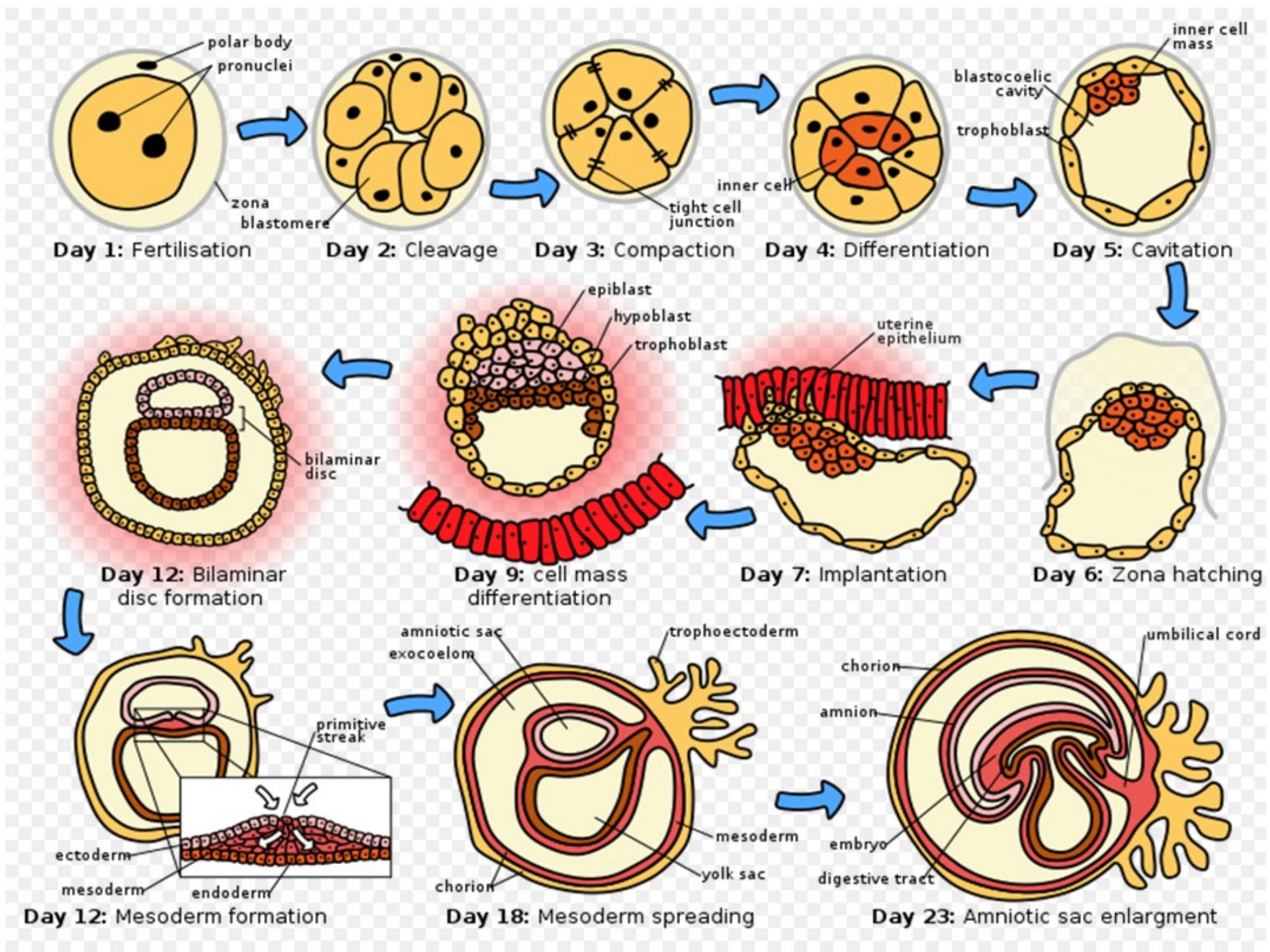

9^2 w


Embryo
Blastocyst
Embryonic stem cell
Embroid body
Hemangioblast
Hematopoietic stem cell
Lymphoid progenitor cell
Lymphoid
Myeloid progenitor cell
Myeloid
Angioblast
Capillaries
Endothelium
AGM region
Yolk sac
Blood island



CURVE DI CRESCITA DI DIVERSE PARTI E TESSUTI DEL CORPO
da TANNER, 1962

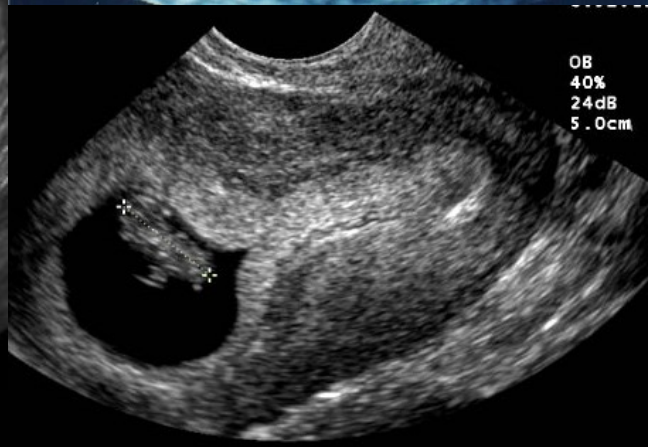


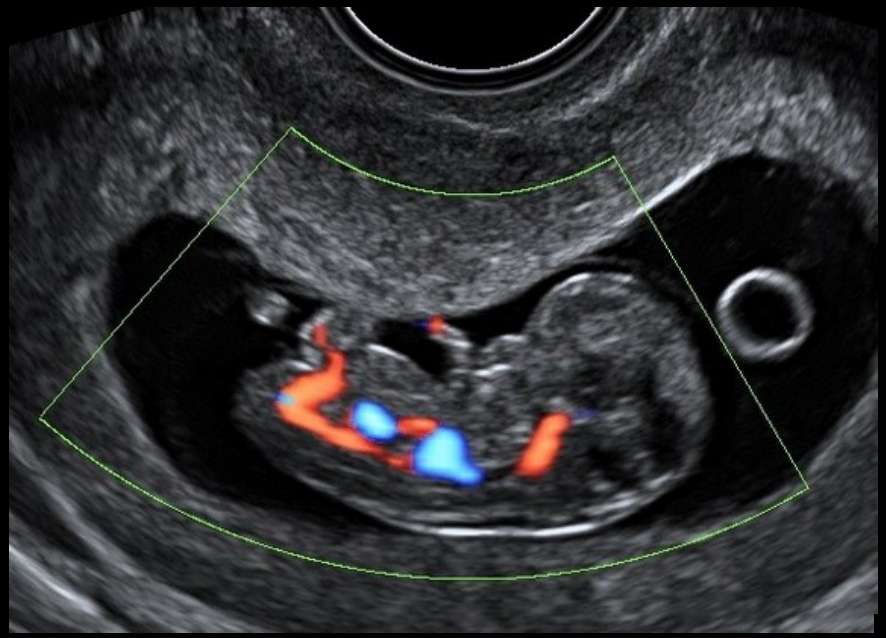

polar body
pronuclei
zona
blastomere
tight cell junction
inner cell
blastocoelic cavity
trophoblast
inner cell mass
Day 1: Fertilisation
Day 2: Cleavage
Day 3: Compaction
Day 4: Differentiation
Day 5: Cavitation
Day 6: Zona hatching
uterine epithelium
Day 7: Implantation
epiblast
hypoblast
trophoblast
Day 9: cell mass differentiation
bilaminar disc
Day 12: Bilaminar disc formation
primitive streak
ectoderm
mesoderm
endoderm
Day 12: Mesoderm formation
amniotic sac
exocoelom
trophoectoderm
mesoderm
yolk sac
chorion
Day 18: Mesoderm spreading
chorion
amnion
umbilical cord
embryo
digestive tract
Day 23: Amniotic sac enlargment

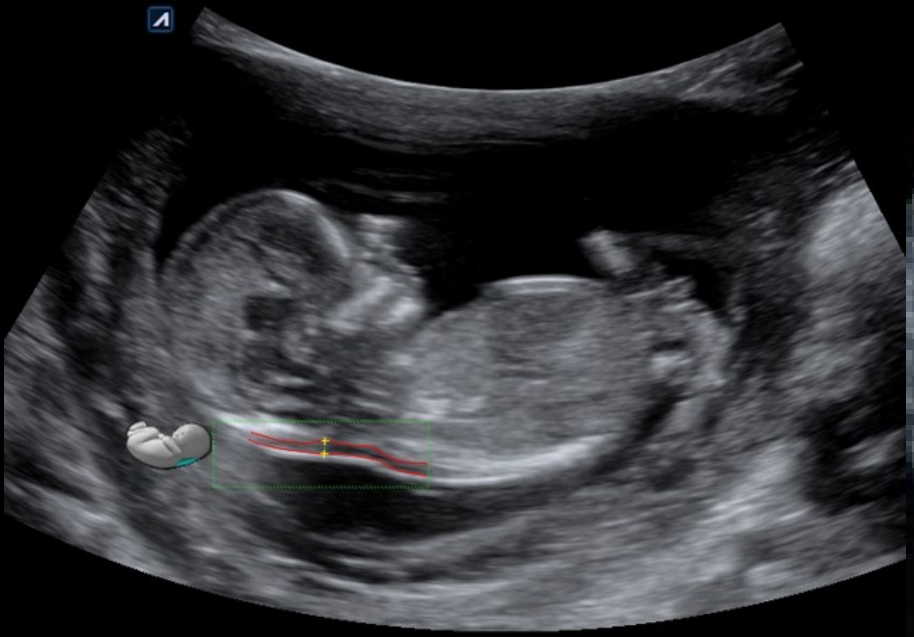

Single

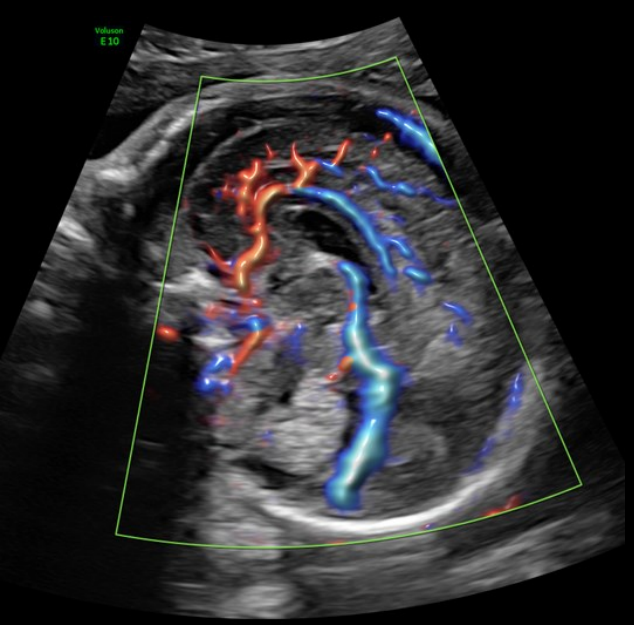

OB
40%
22dB
5.0cm
RS4
54fps

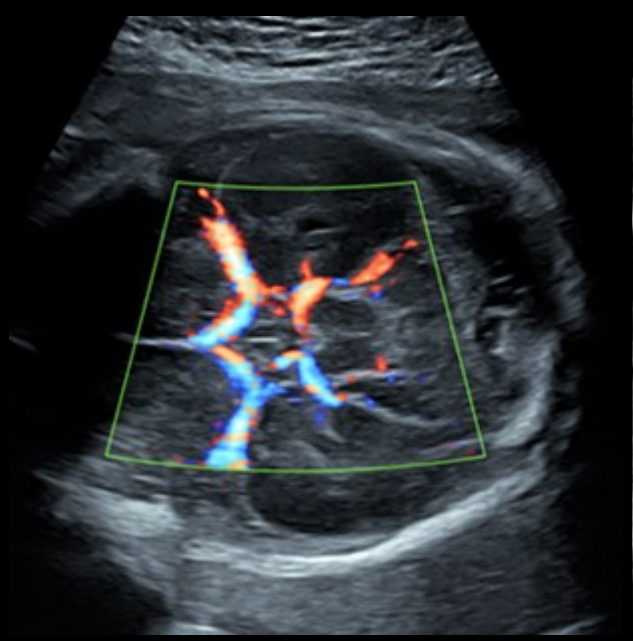

BABY
A
BABY
B

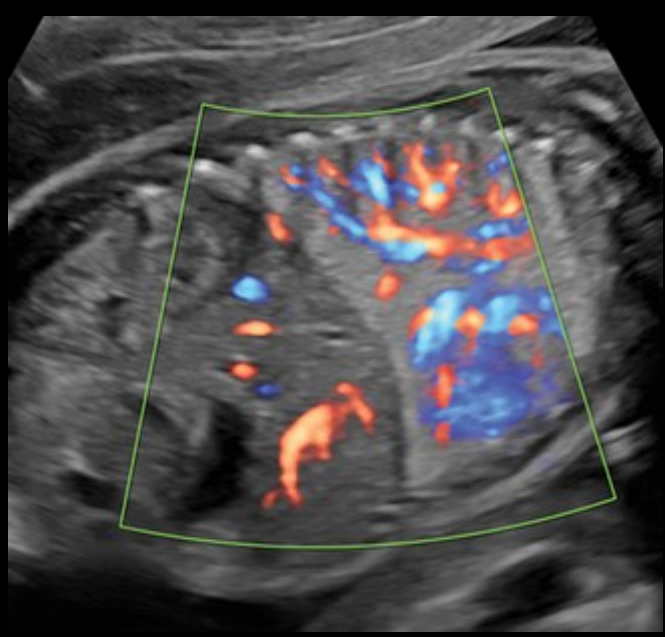

OB
40%
24dB
5.0cm

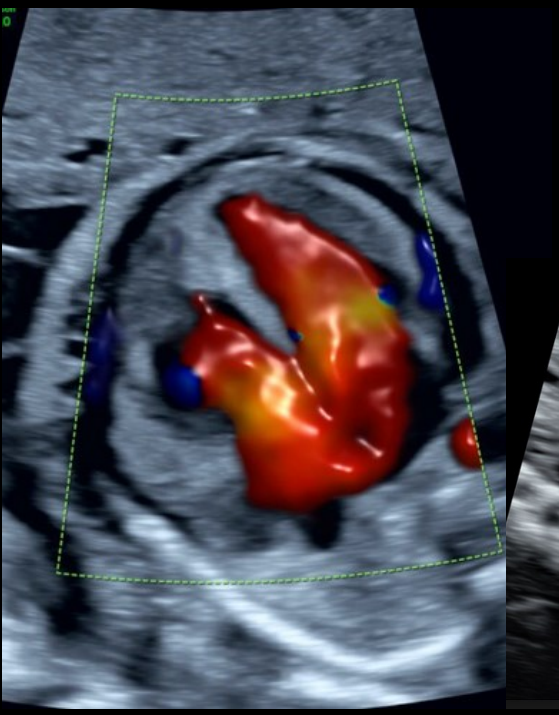


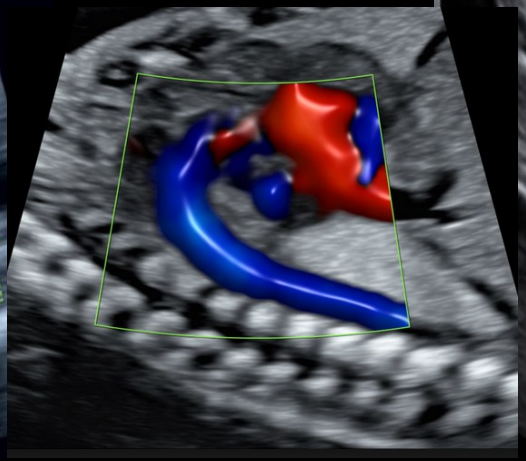



Voluson
E10

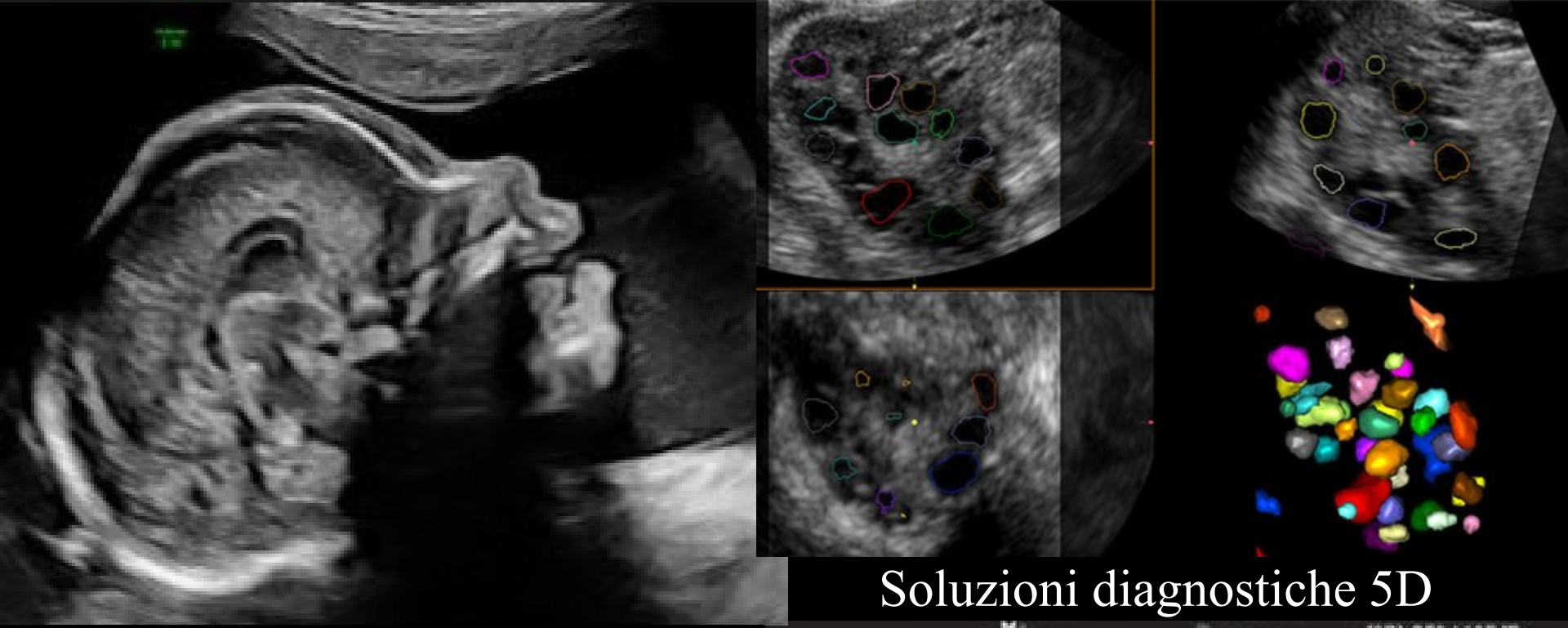




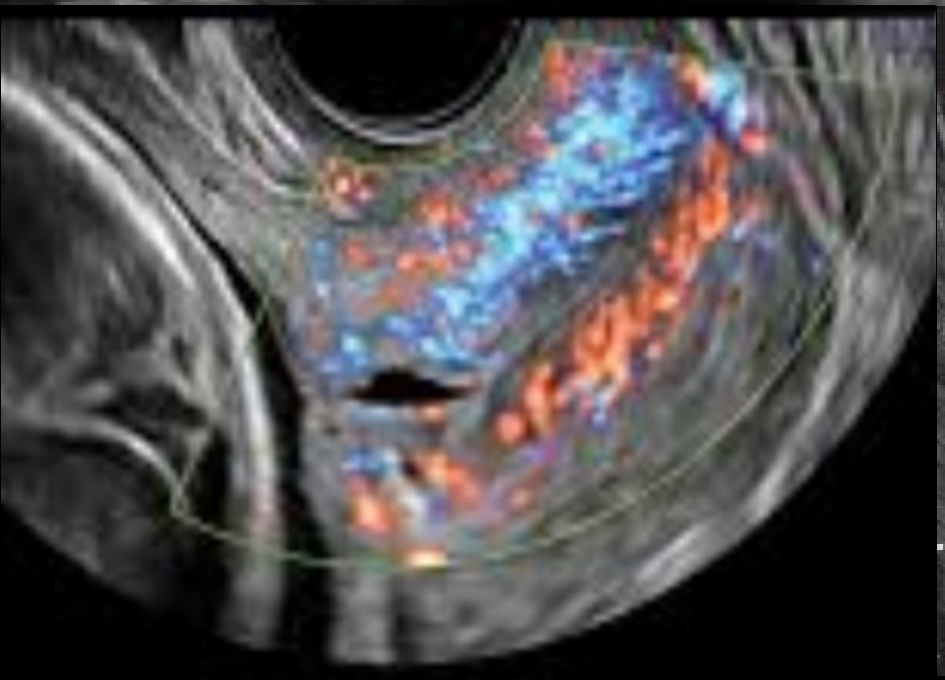


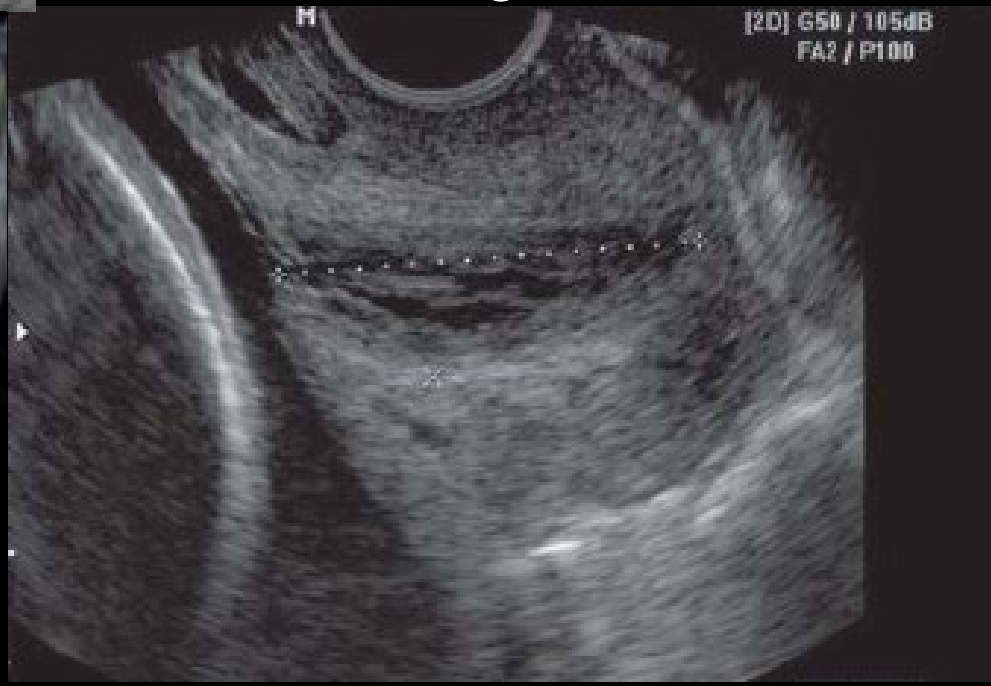


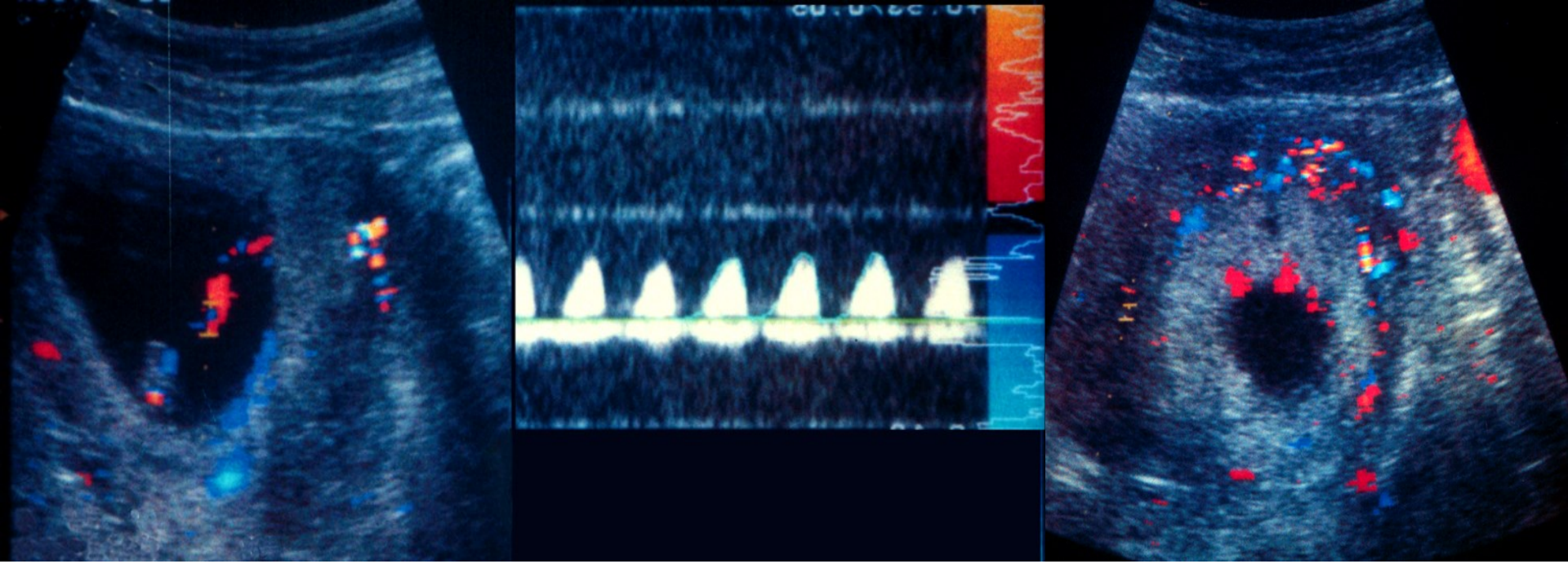

Har-high
Pwr 100
Gn -12
C6 / M2
P1 / E0

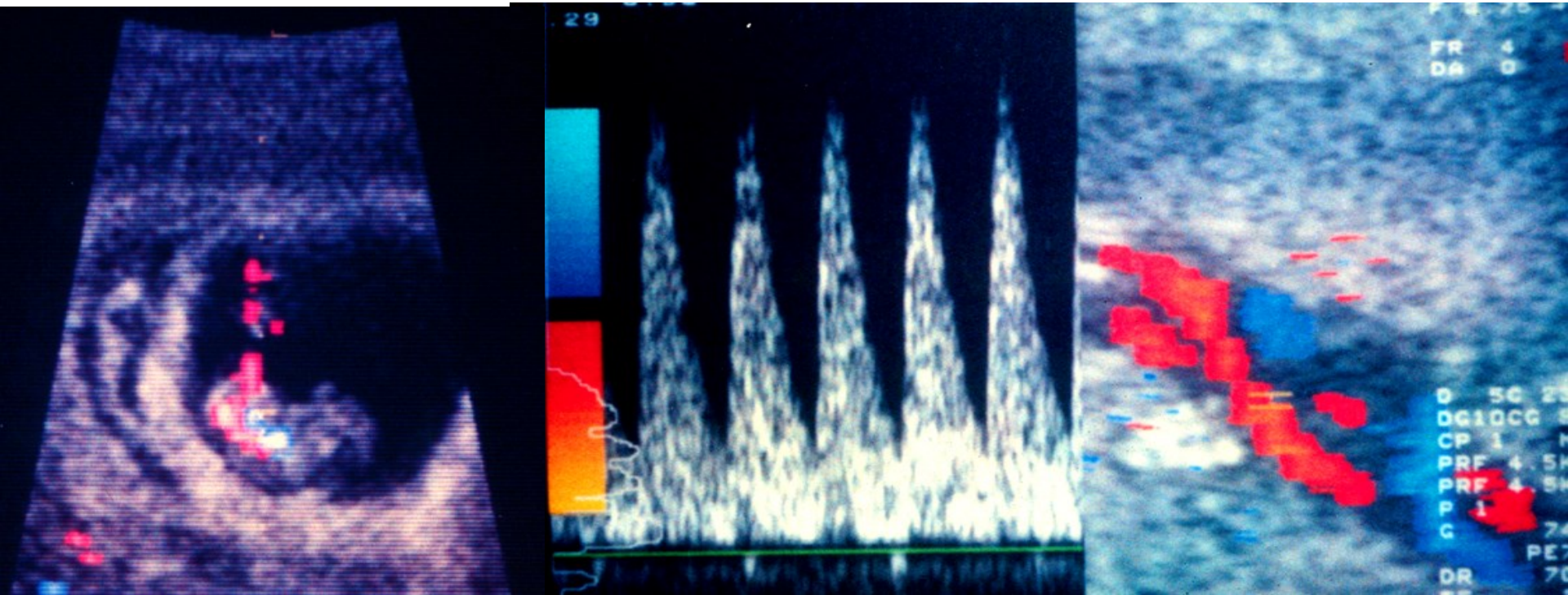


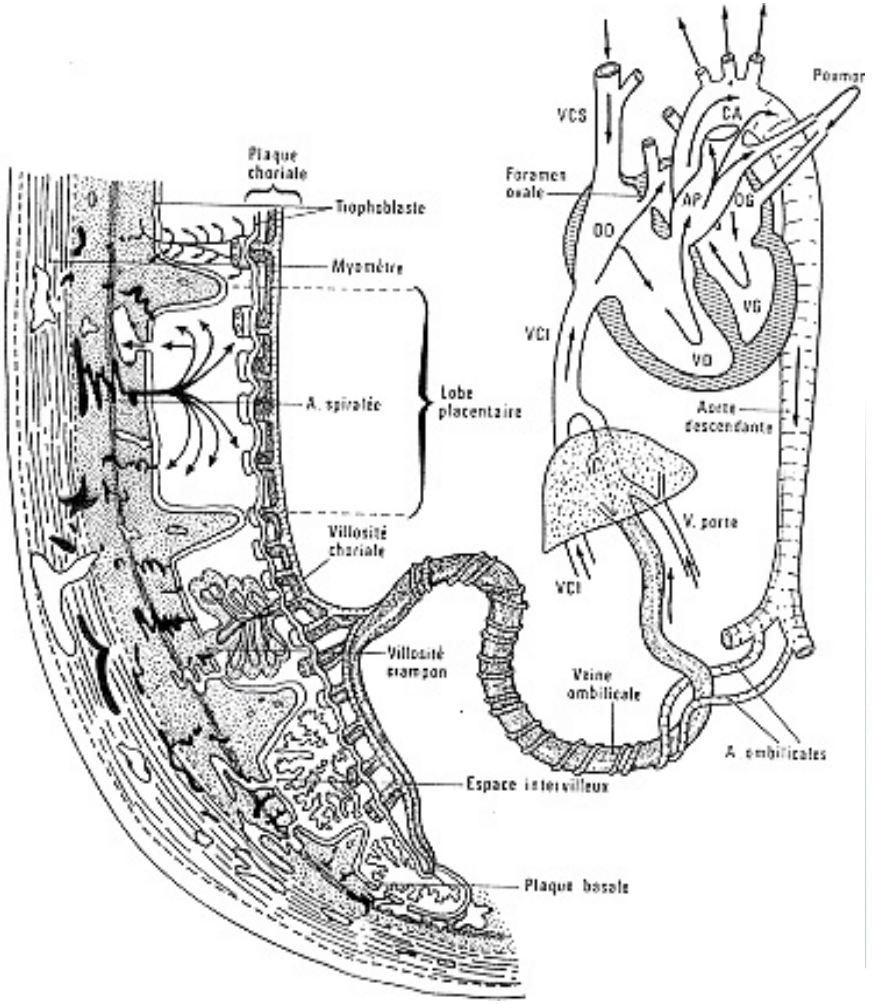
Soluzioni diagnostiche 5D

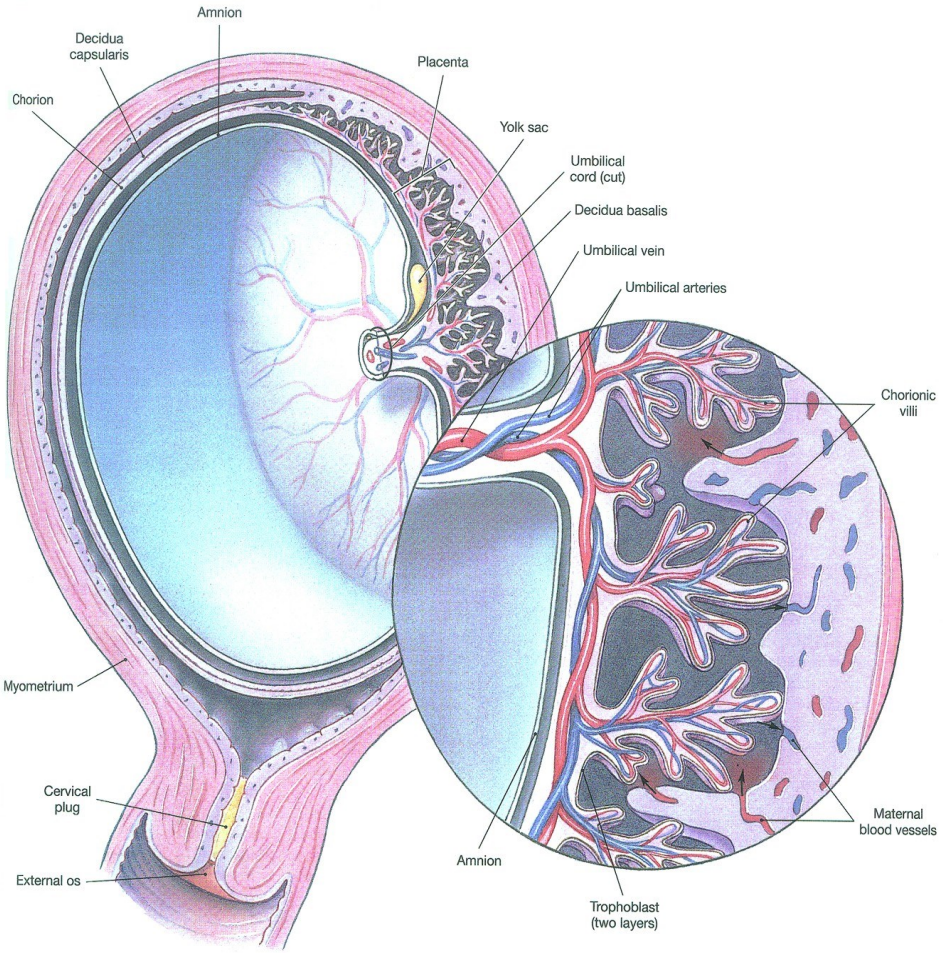







29
FR 4
DA 0
DG10CG
CP 1
PRF 4.5
PRF 4.5
P 1
G
DR


Plaque choriale
Trophoblaste
Myomètre
A. spiralée
Lobe placentaire
Villosité choriale
Villosité crampon
Espace intervilleux
Plaque basale
Foramen ovale
VCS
OD
VCI
VD
AP
OG
VG
Poumon
Aorte descendante
V. porte
Veine ombilicale
A. ombilicales


Amnion
Decidua capsularis
Placenta
Chorion
Yolk sac
Umbilical cord (cut)
Decidua basalis
Umbilical vein
Umbilical arteries
Chorionic villi
Myometrium
Cervical plug
External os
Amnion
Maternal blood vessels
Trophoblast (two layers)

Waste Products

carbon dioxide
urea, uric acid
bilirubin

Other Substances

R.B.C. antigens

via umbilical arteries

via umbilical vein

fetal capillary

intervillous space

placental membrane

mother's lungs and kidneys

via endometrial veins

endometrial spiral arteries

Nutrients

oxygen
water
carbohydrates
amino acids
lipids
electrolytes

Other Substances

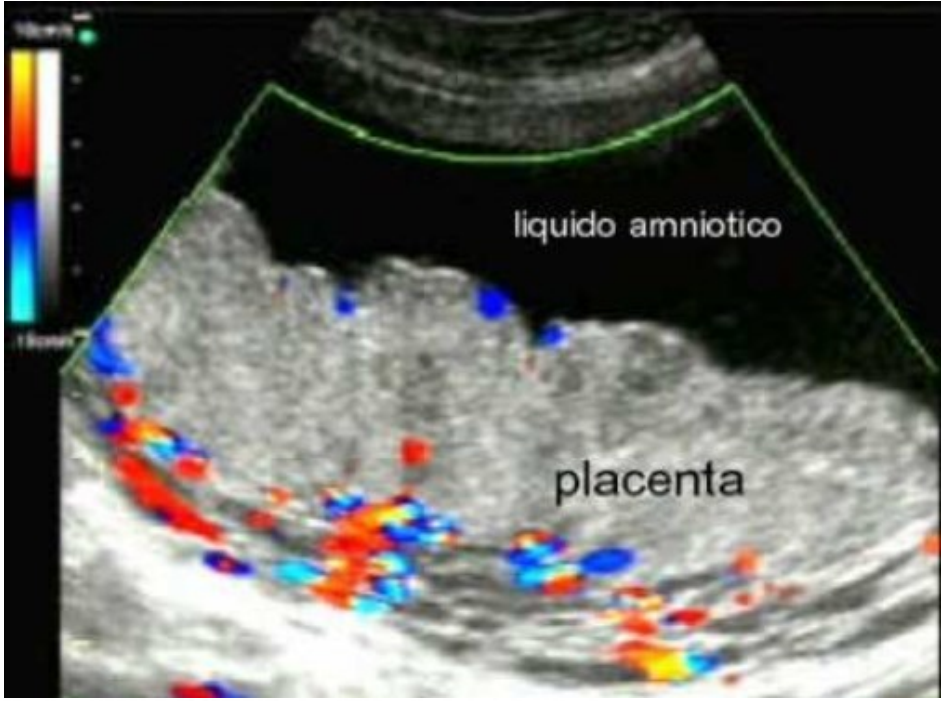
antibodies, IgG & vitamins

Harmful Substances

drugs (e.g., alcohol)
poisons & carbon monoxide
viruses < rubella, cytomegalovirus
strontium-90
(Toxoplasma gondii)

Nontransferable Substances

bacteria, heparin
transferrin, IgS & IgM



AZIENDA OSPEDALIERA PADOVA

REGIONE DEL VENETO

UNITÀ OPERATIVA DI ANATOMIA PATOLOGICA

Direttore Prof. Massimo Rugge

UNIVERSITÀ DEGLI STUDI PADOVA

Accettazione 14/04/2014
Refertazione 01/05/2014
Cod. Paziente 47363226

CLINICA GINECOLOGICA OSTETRICA

Referto n° 14-17462
Pag. 1/1
Data di nascita 14/04/1975

DESCRIZIONE MACROSCOPICA

REPERTO MACROSCOPICO (campione pervenuto fissato in formalina) [SC]:
Materiale inviato in esame come "placenta e membrane" del peso di g 375 e delle dimensioni di cm 11 x 12, d
forma rotondeggiante. Funicolo (lungo cm 28) presenta 2 varici simmetriche poste a cm 8 dall'inserzione. E
presente banda amniotica che risale per cm 4 dall'inserzione con una base di cm 3. In sezione sono presenti
vasi.
Le membrane sono ispessite e di colorito beige-giallastro.
Il versante fetale è spalmato di scarso materiale simil-purulento, un vaso del piatto coriale sembra chiuso.
Il versante materno presenta area marginale di necrosi con coaguli di circa di cm 6 x 3.
Al taglio non si repertano lesioni a focolaio. Si preleva:
1) materiale presente alla superficie amniotica
2) funicolo
3-4) membrane

DIAGNOSI

Corioamnionite, grave ed estesamente necrotizzante l'epitelio amniotico, con aggregati purulenti anche alla superficie interna del sacco amniotico, e con estensione della flogosi al connettivo del piatto coriale, con vasculite e focale trombosi dei vasi del piatto coriale, vasculite e perivasculite del funicolo, e focolaio marginale di necrosi della decidua e dei villi con stratificazione di aggregati ematici e purulenti. Diffusa irregolarità del calibro degli spazi reticolari dello stroma dei villi; alterazioni di tipo regressivo delle fibre dei vasi. (1-10)

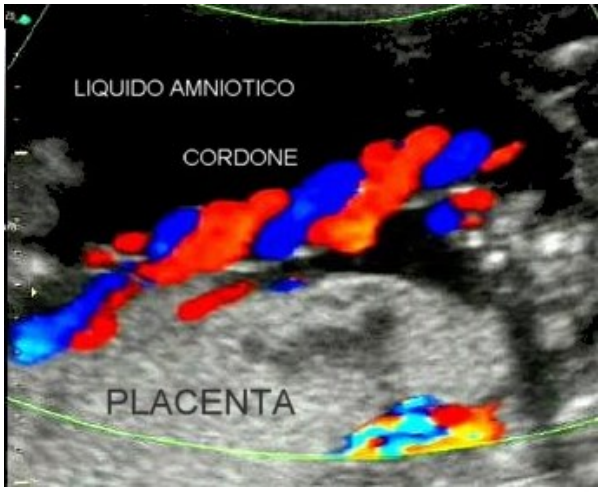
(Si raccomanda stretta sorveglianza microbiologica in eventuale successiva gravidanza)

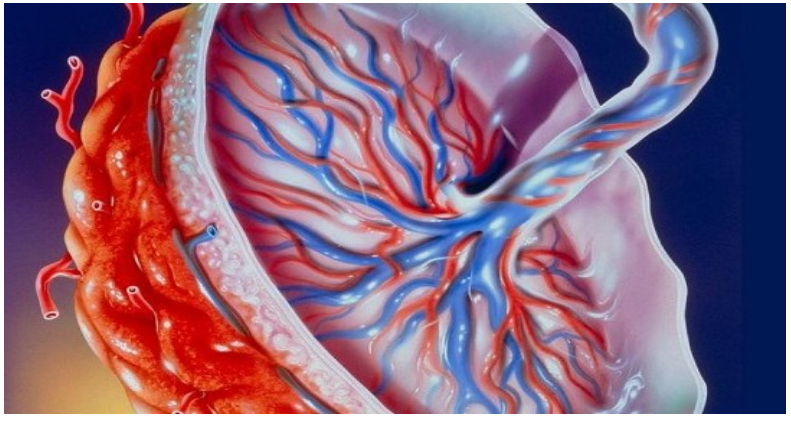
L'esaminatore: Prof.ssa S. Chiarelli : /SC

16 OTT. 2014

(Prof. M.Rugge)

REGIONE DEL VENETO
AZIENDA OSPEDALIERA DI PADOVA
Clinica Ginecologica e Ostetrica
OSTETRICIA
Direttore: Prof. G.B. NARDELLI





Cordone Ombelicale:
2 Arterie ed 1 vena

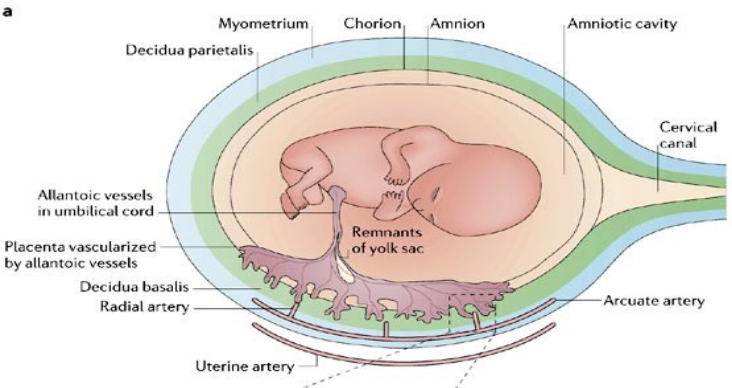
Vascolarizzazione
feto-placentare

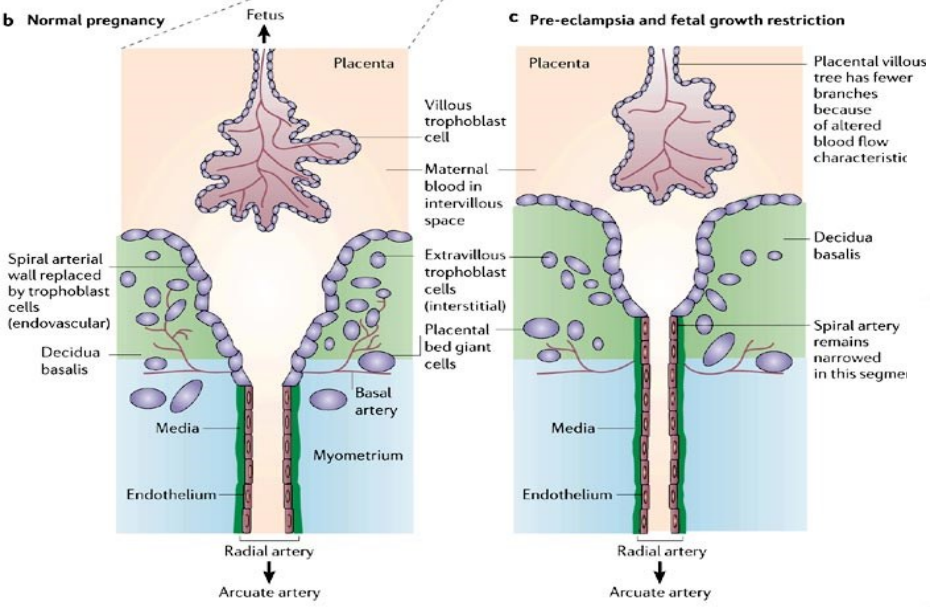
Villi coriali
arborizzati e
vascolarizzati

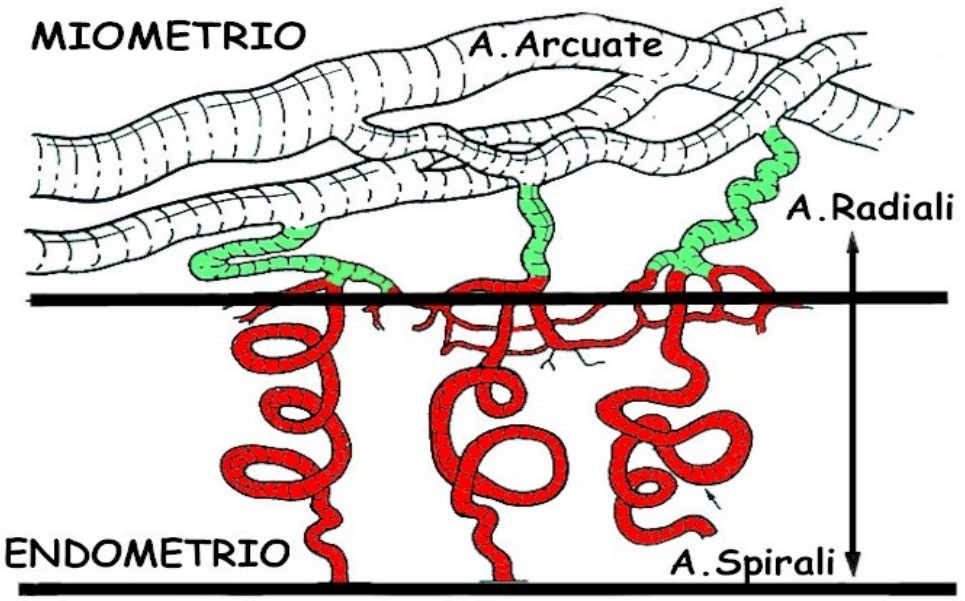
Art.Uterine
Art.Arcuate
Art.Radiali
Art.Spirali

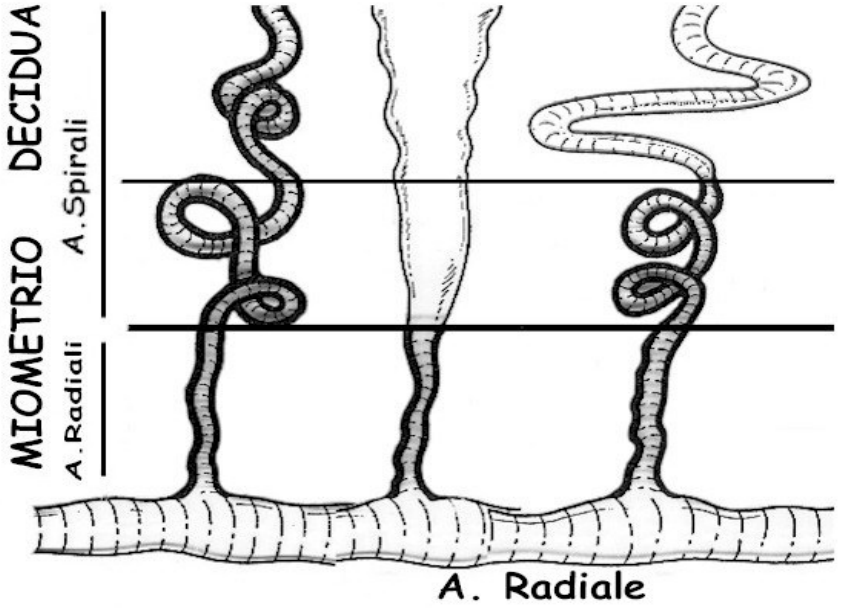
Vascolarizzazione
utero-placentare

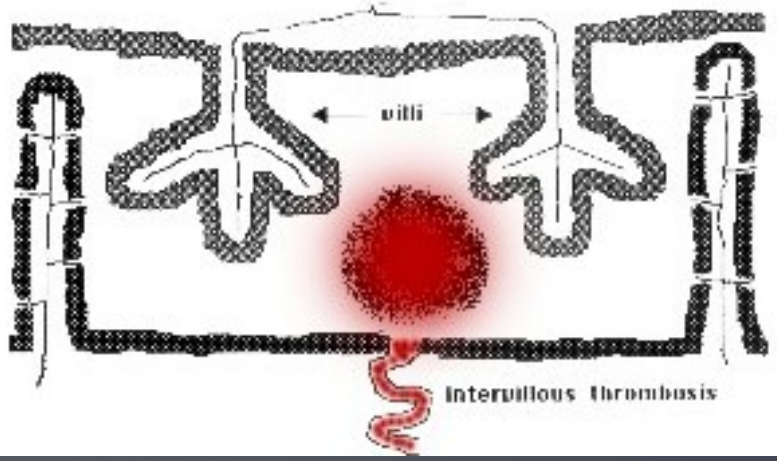
Lacune
placentari

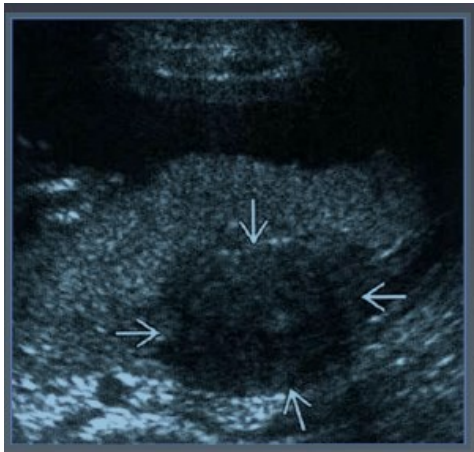




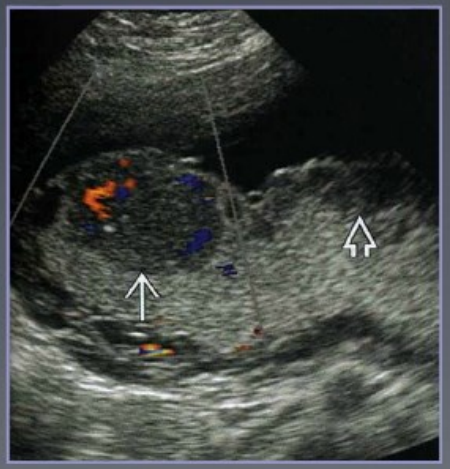




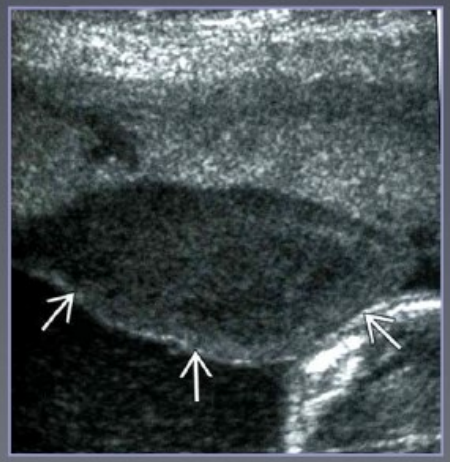




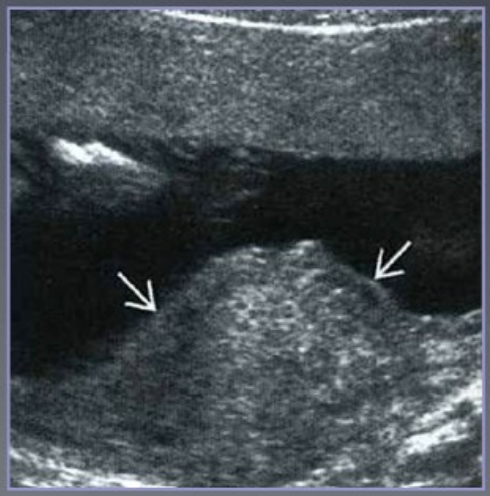
FIBROMA



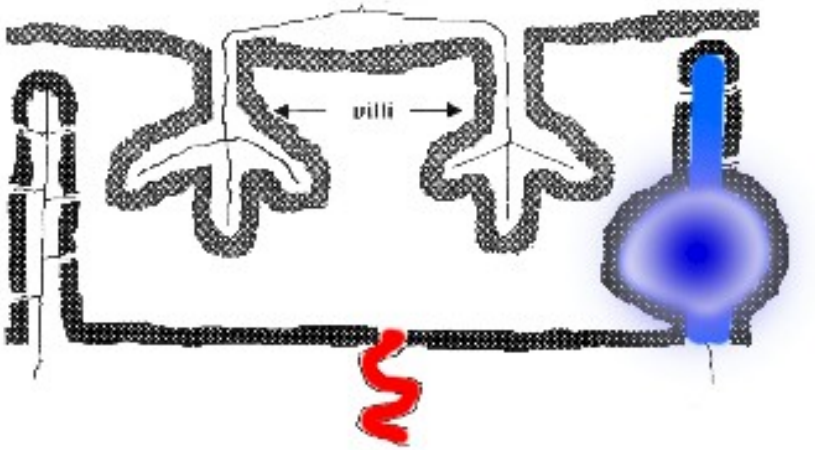
CORIONANGIOMA

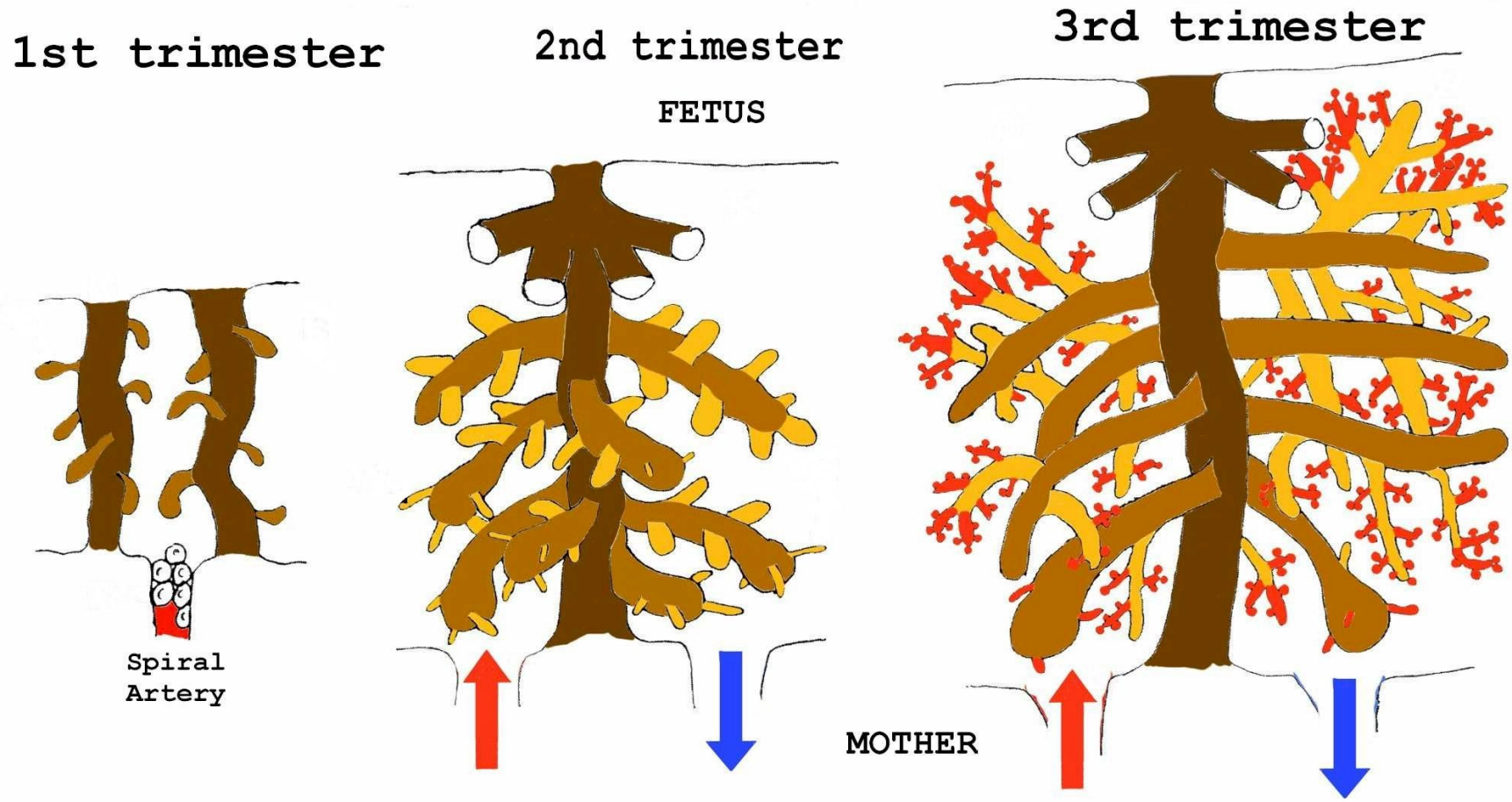


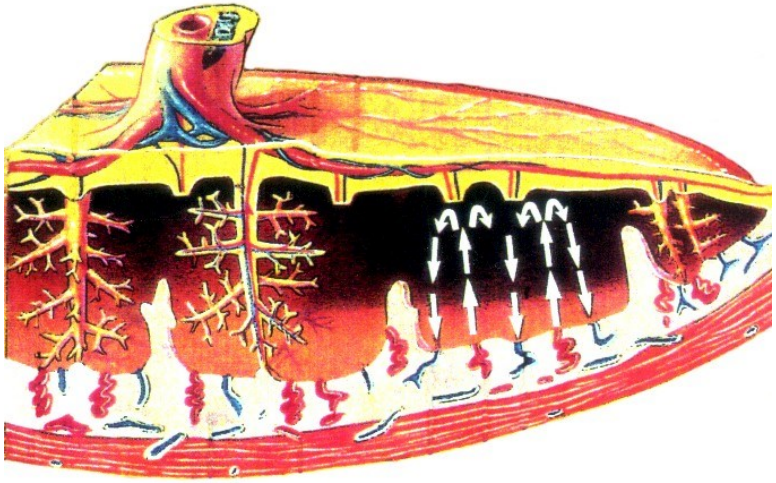
LACUNA VASCOLARE

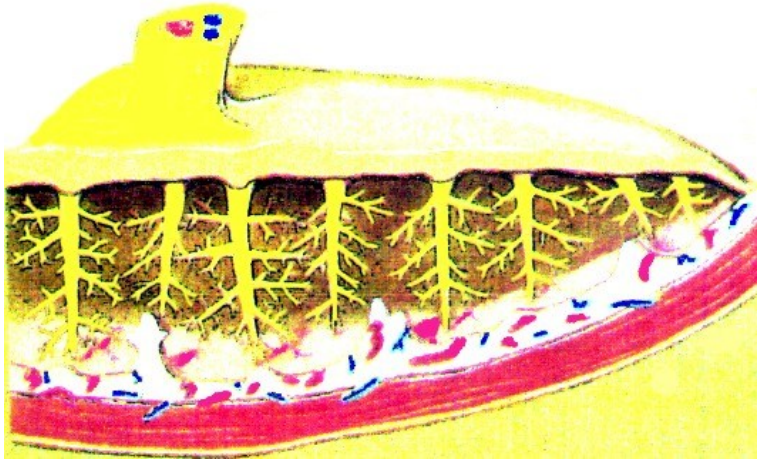


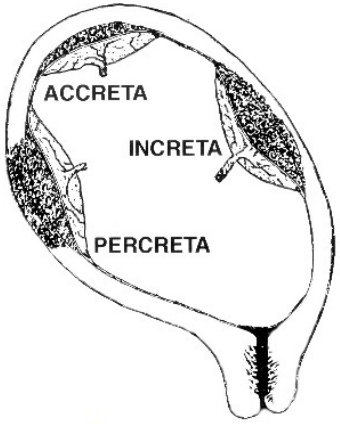
CONTRAZIONE

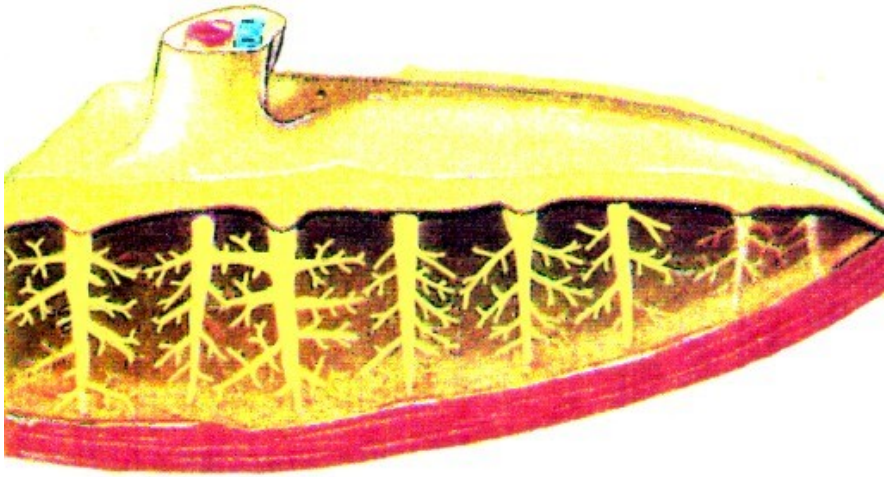


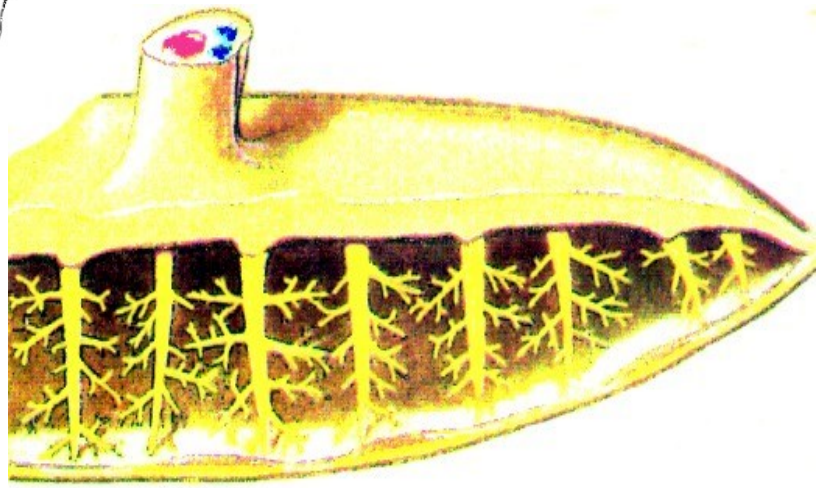

1st trimester
2nd trimester
3rd trimester
FETUS
Spiral
Artery
MOTHER

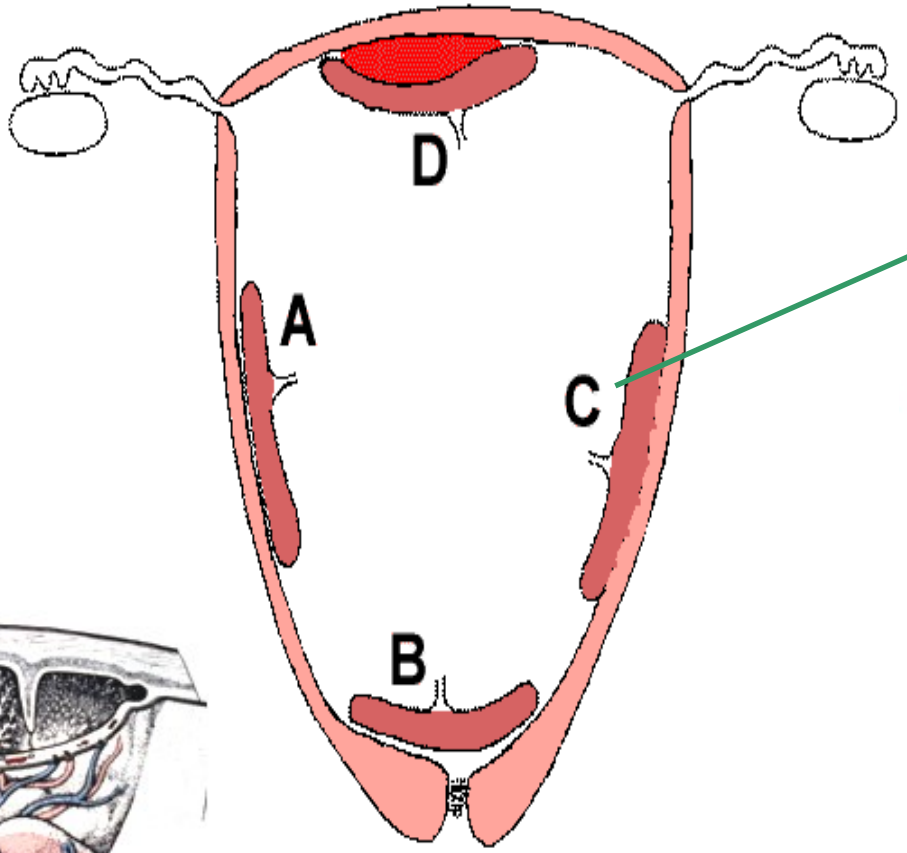


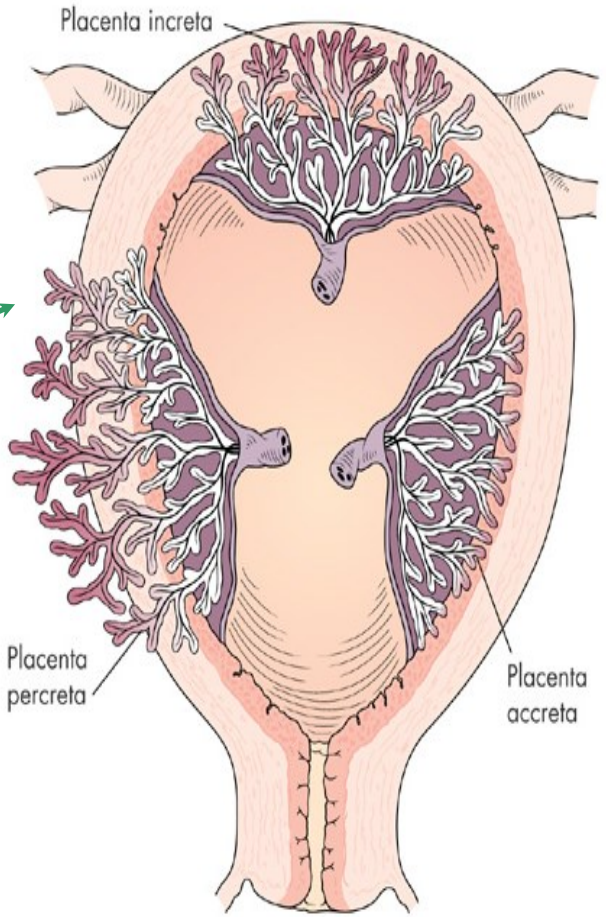



ACCRETA
INCRETA
PERCRETA









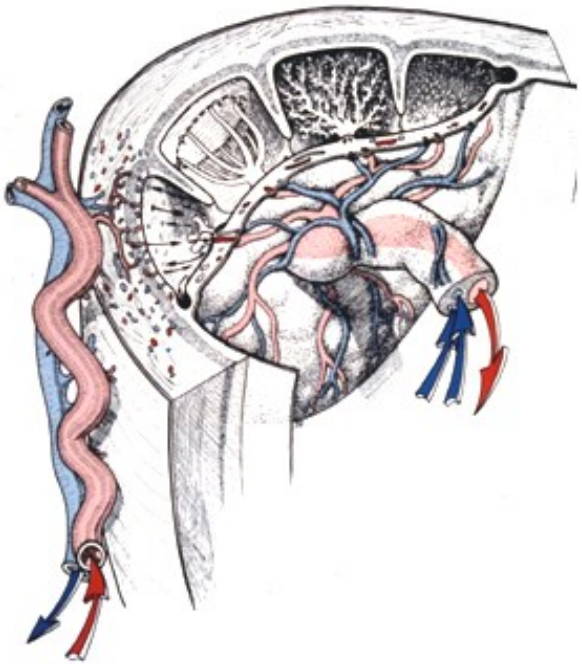
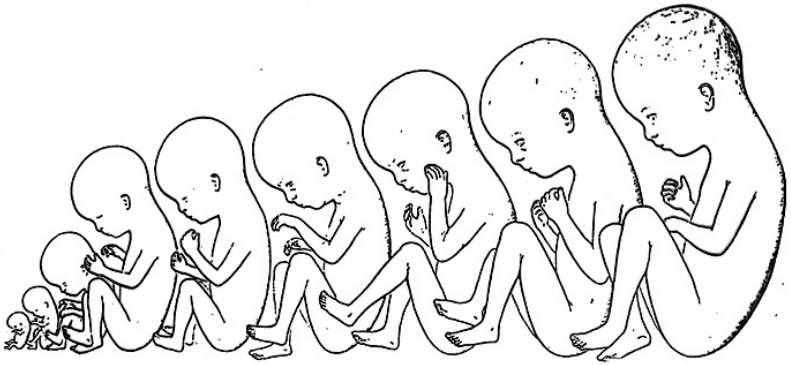
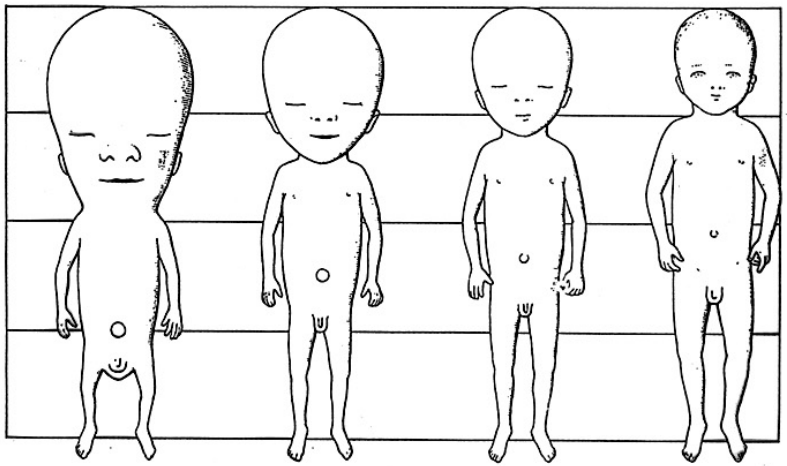
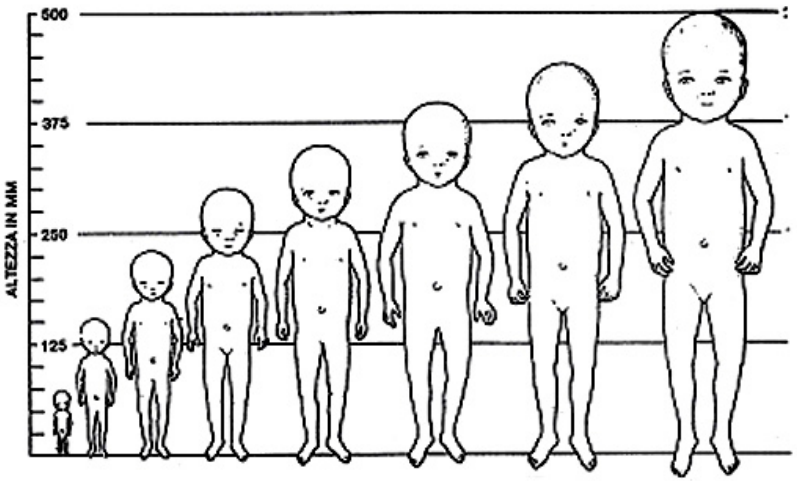
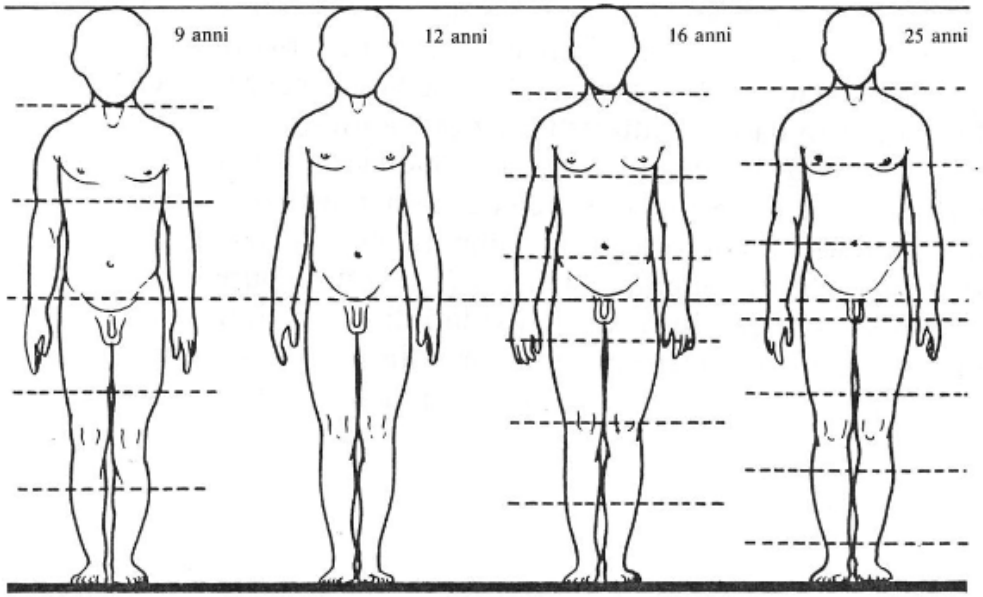


Fig. 1. — Circolazione fetale e materna nella placenta umana

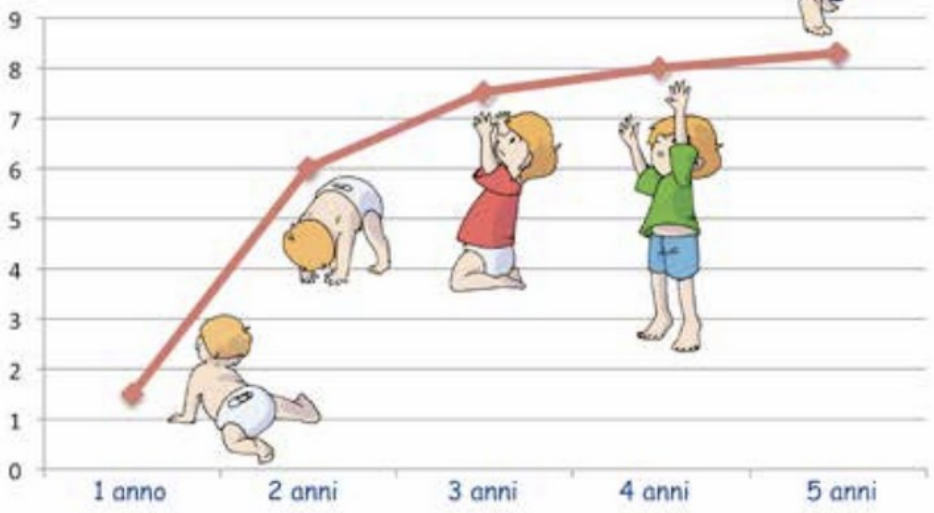





500
375
250
125
ALTEZZA IN MM


9 anni
12 anni
16 anni
25 anni

Auxologia


9
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1 anno
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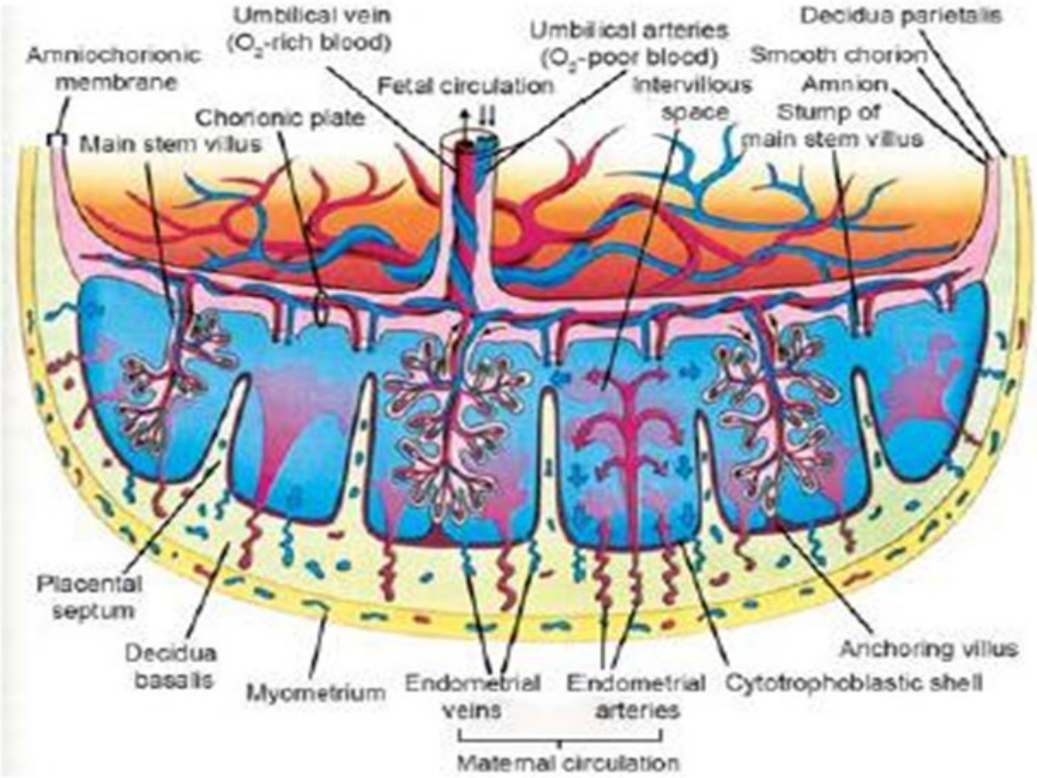

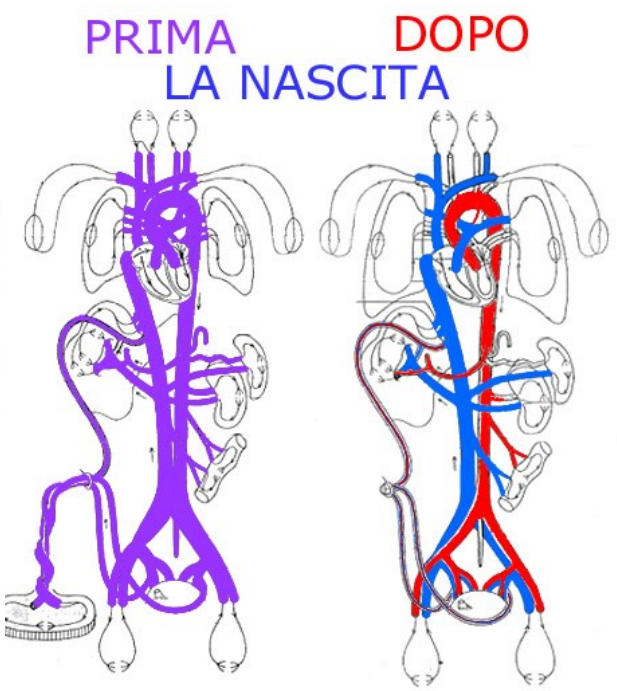

LA PLACENTA
…. il più perfetto
by-pass intracorporeo
tramite neo-angiogenesi
temporanea ….