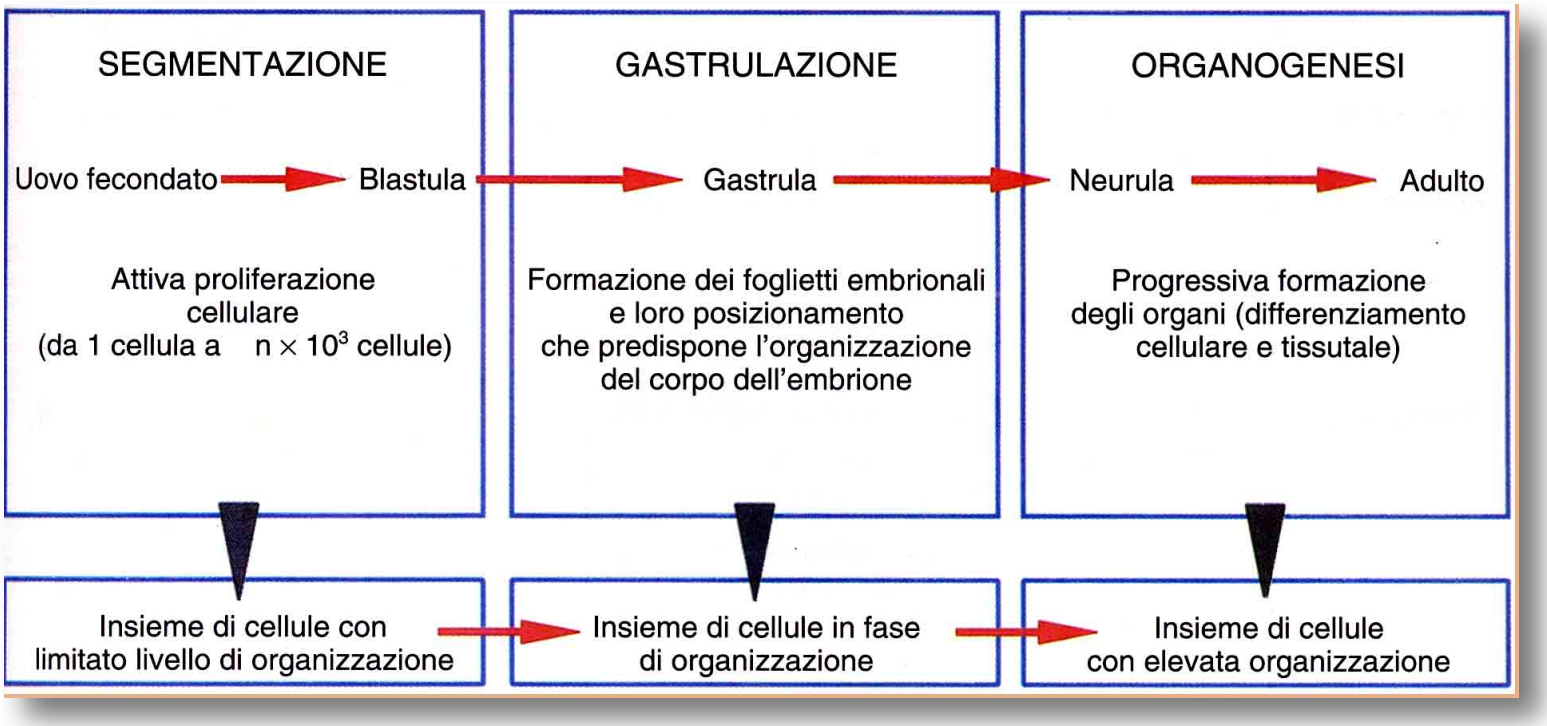
SVILUPPO EMBRIONALE

Prevede processi quali:



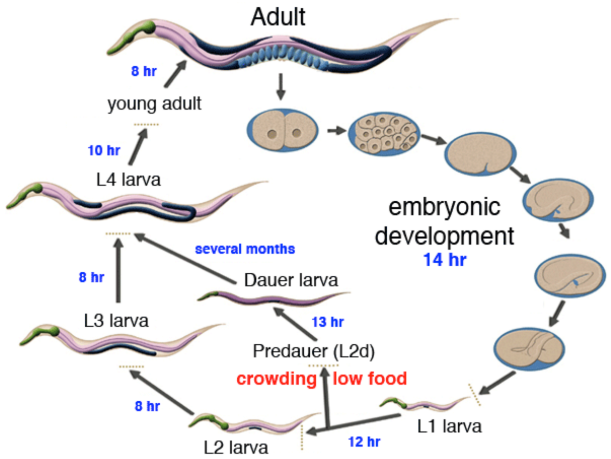
...ed è regolato dall'azione di:

Geni materni → Geni "*Master*" regolatori → Geni esecutori

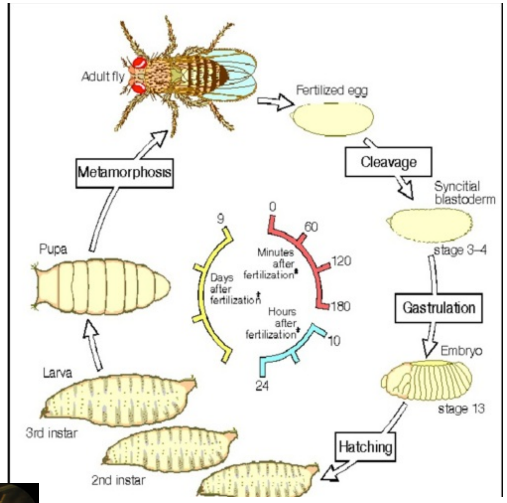
SVILUPPO EMBRIONALE

Modelli sperimentali

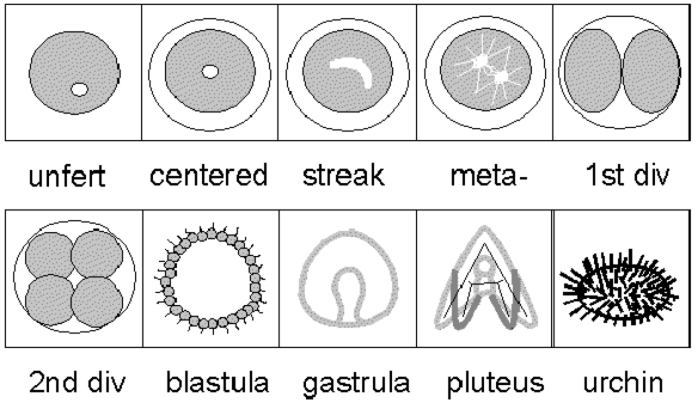
Invertebrati

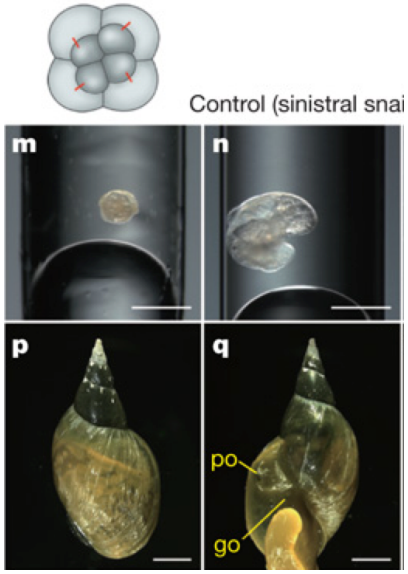


Chaenorabditis elegans



Drosophila melanogaster





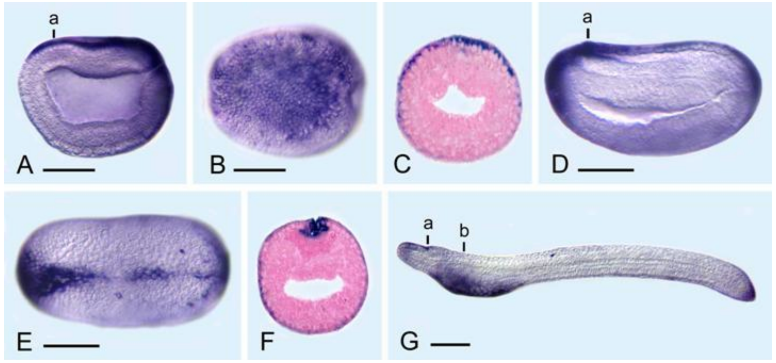
Gasteropodi

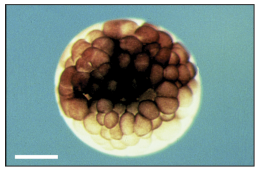
Riccio di mare

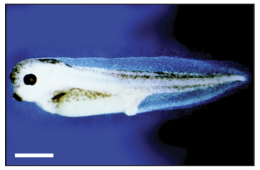
SVILUPPO EMBRIONALE

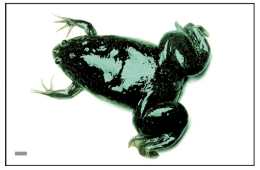
Modelli sperimentali

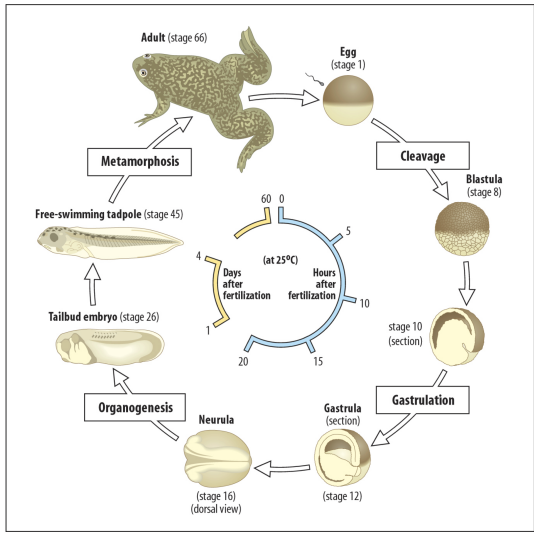
Anfiosso



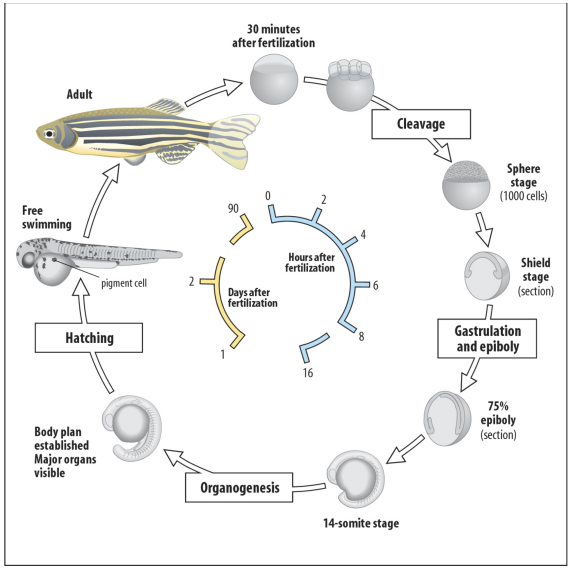


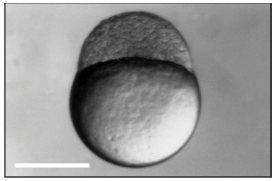


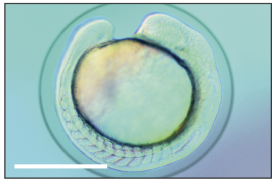


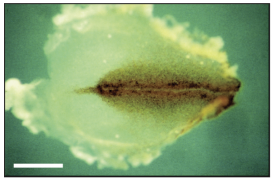


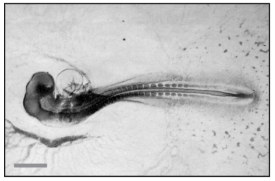
Anfibi (Xenopus laevis)

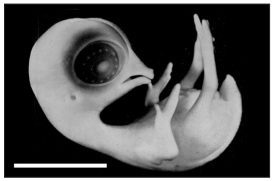


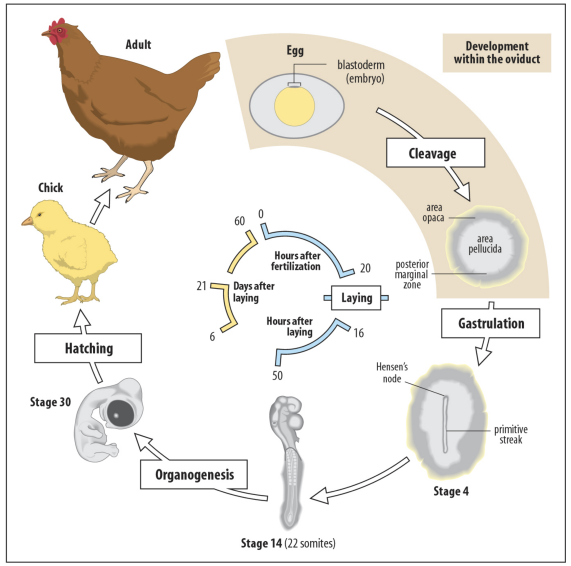










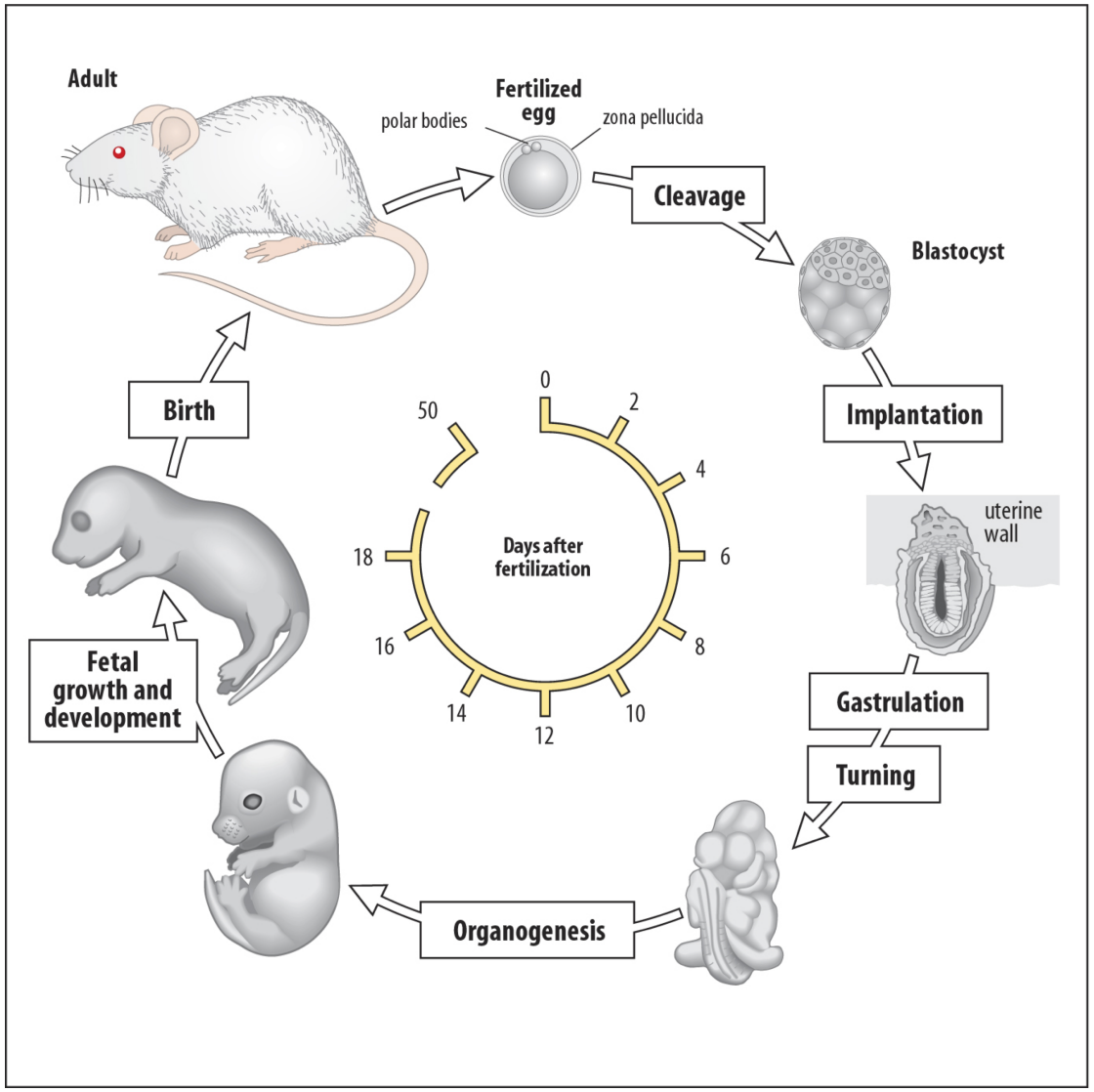


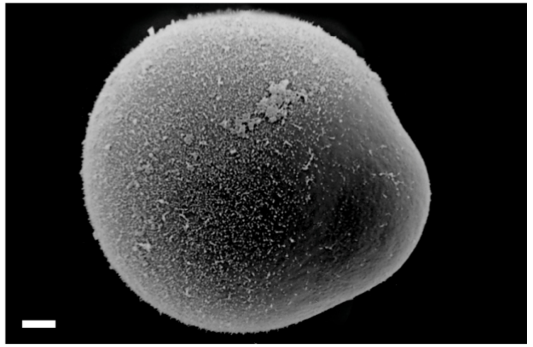
Pesci (zebrafish)

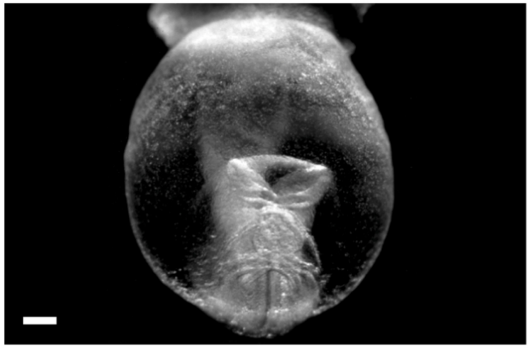
Uccelli (e rettili) (Gallus gallus)

SVILUPPO EMBRIONALE

Modelli sperimentali



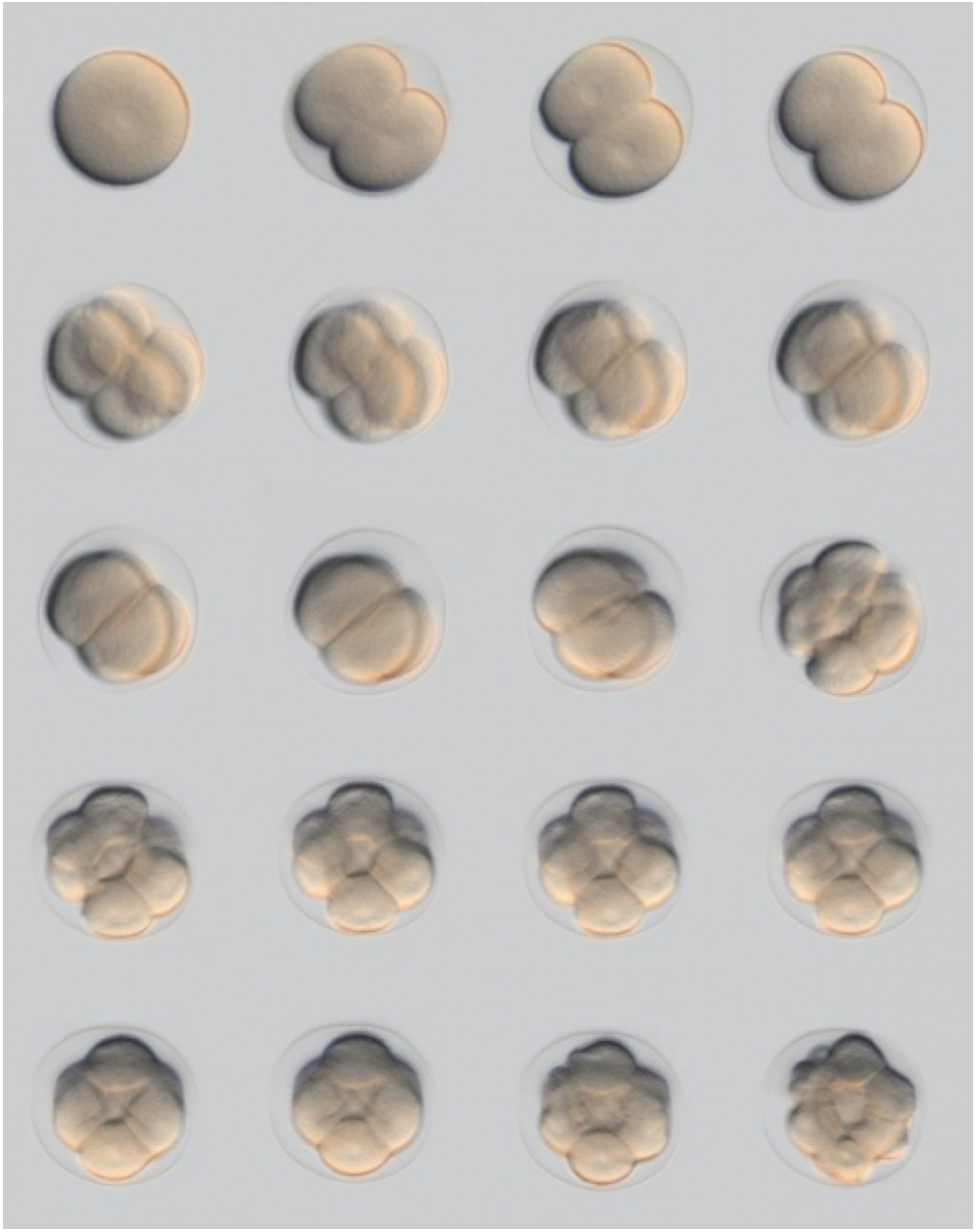




Mammiferi placentati (Mus musculus)

LA SEGMENTAZIONE

La segmentazione (in inglese CLEAVAGE) comporta la pluricellularità dello zigote. Le cellule che si originano vengono dette *blastomeri* e derivano da mitosi particolari in cui manca la fase di accrescimento, per cui esse diventano progressivamente più piccole fino a ristabilire un rapporto nucleo-citoplasmatico tipico delle specie, rapporto che nell'uovo è fortemente spostato a favore del citoplasma



What is cleavage?

Cleavage is a rapid series of mitotic divisions that occur just after fertilization.

There are two critical reasons why cleavage is so important:

1. **Generation of a large number of cells that can undergo differentiation and gastrulation to form organs.**
2. **Increase in the nucleus / cytoplasmic ratio. Eggs need a lot of cytoplasm to support embryogenesis. It is difficult or impossible for one nucleus to support a huge cytoplasm, and oocytes are one of the largest cells that exist. One small nucleus just cannot transcribe enough RNA to meet the needs of the huge cytoplasm.**

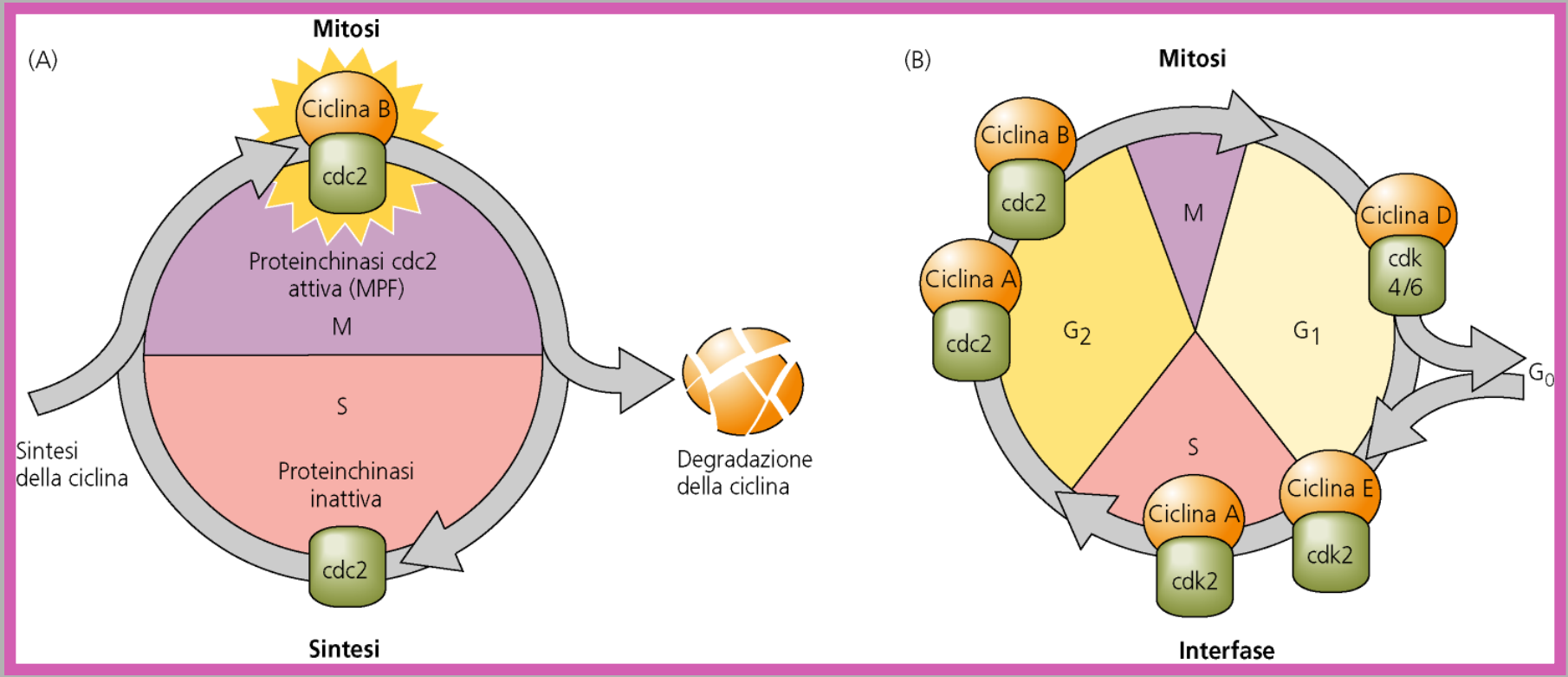
A larger nucleus to cytoplasmic ratio is optimal for cell function. Cell division occurs rapidly after fertilization to correct this problem.

Cleavage differs from normal mitoses in 2 respects

1. Blastomeres do not grow in size between successive cell divisions as they do in most cells. This leads to a rapid increase in the nucleus / cytoplasmic ratio. Cells undergoing cleavage have mainly S and M phases of the cell cycle (little or no G1 or G2).
2. Cleavage occurs very rapidly, and mitosis and cytokinesis in each round of cell division are complete within an hour. Typical somatic cells divide much more slowly (several hours to days) and even the fastest cancer cells divide much slower than occurs in a zygote during cleavage.

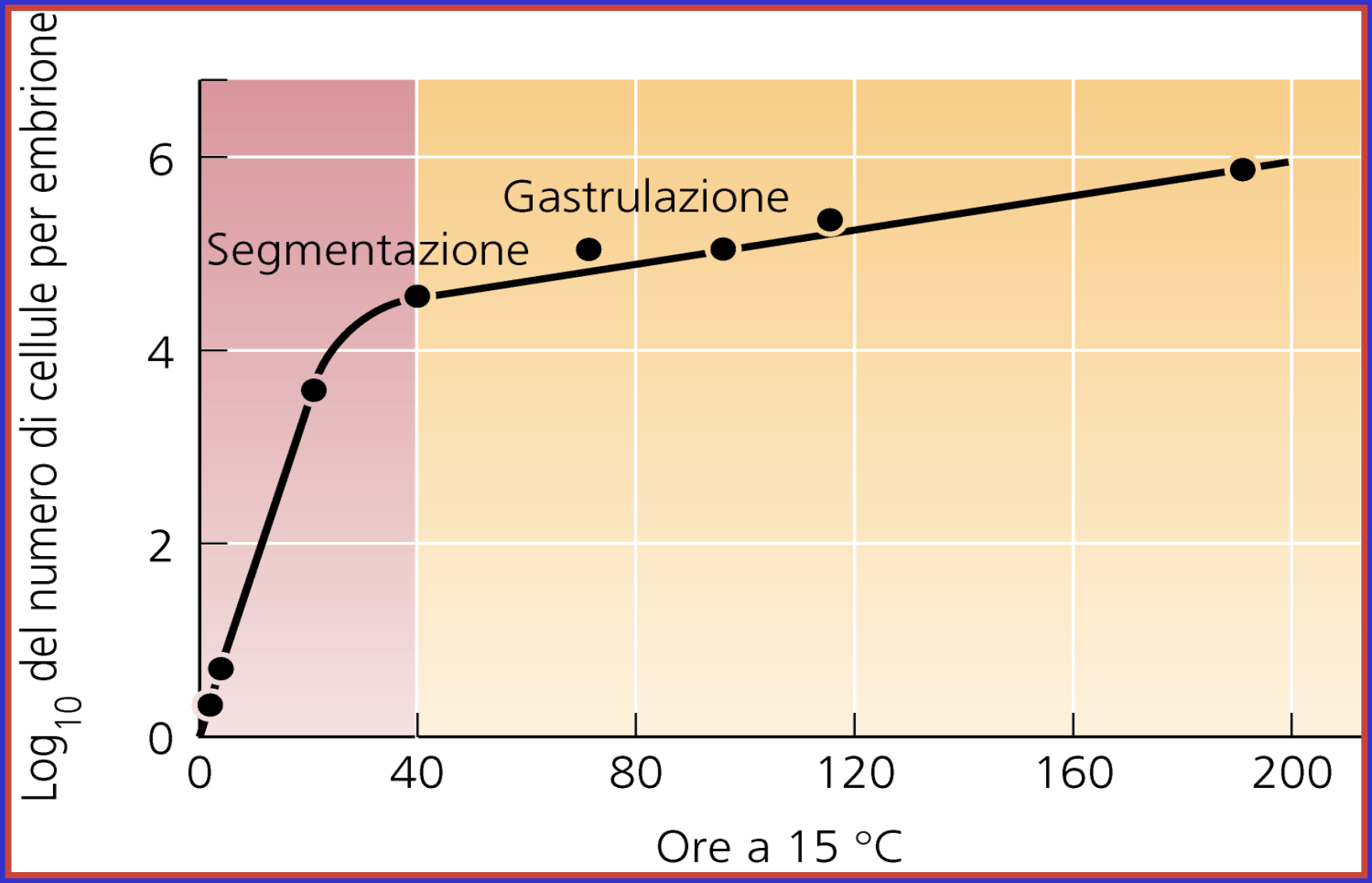
Cleavage differs in different types of eggs. The presence of large amounts of yolk alters the cleavage pattern, leading to incomplete cleavage that characterizes birds and reptiles.

Ciclo cellulare durante la segmentazione:
confronto tra il ciclo nei blastomeri e nelle cellule somatiche



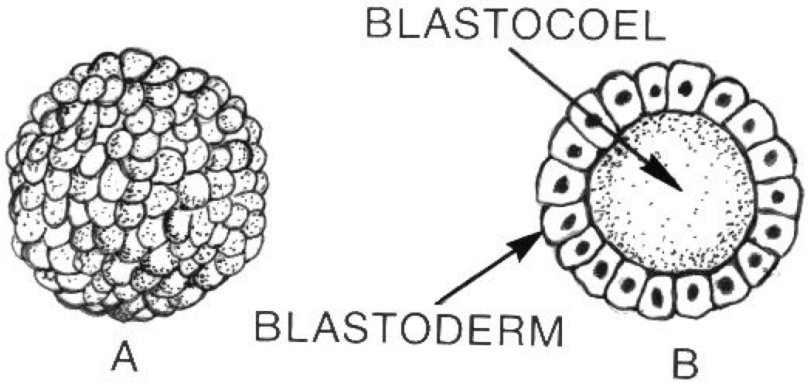
Nei blastomeri (a sinistra) mancano le fasi G1 e G2. La sintesi della ciclina determina la fase M, la sua degradazione l'ingresso in fase S

Ritmo di formazione dei blastomeri

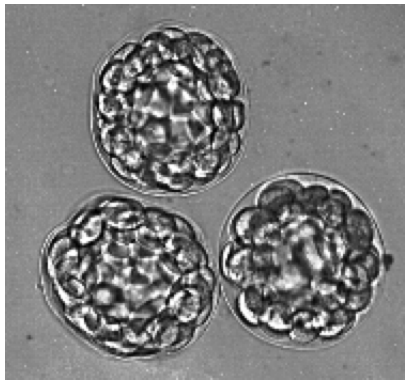


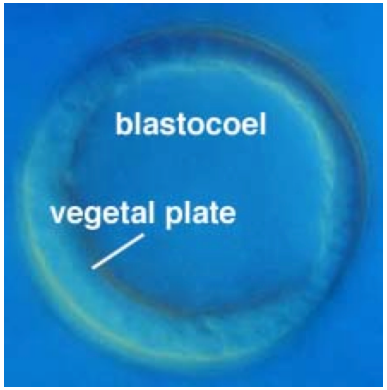
Ritmo di formazione dei blastomeri

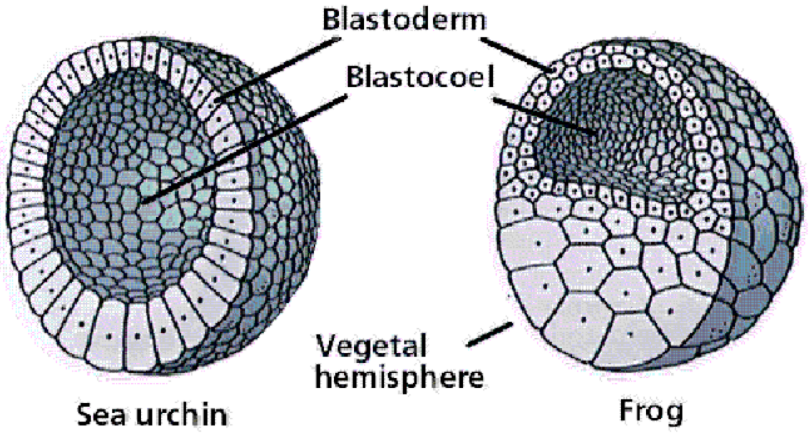
Le mitosi si susseguono rapidamente: nella rana si raggiungono 37000 cellule in 40 ore; in drosofila ogni 9-10 minuti avviene una mitosi e si ottengono 50000 cellule in 12 ore. Con gli stadi finali della segmentazione (*Transizione di medioblastula)* il ritmo di divisioni diminuisce ed esse diventano asincrone, i blastomeri diventano mobili e spesso formano protuberanze.



Alla fine della segmentazione si raggiunge lo stadio di blastula, che può presentare una cavità piena di liquido, il *blastocele.*



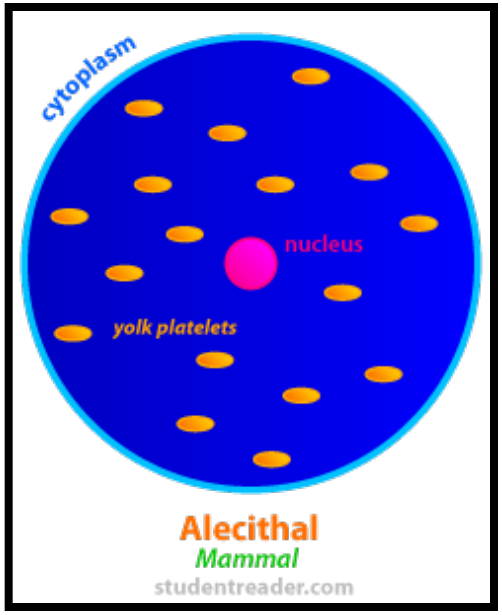


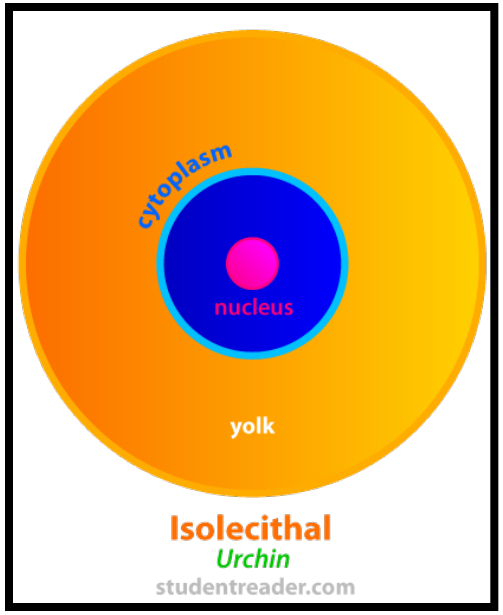


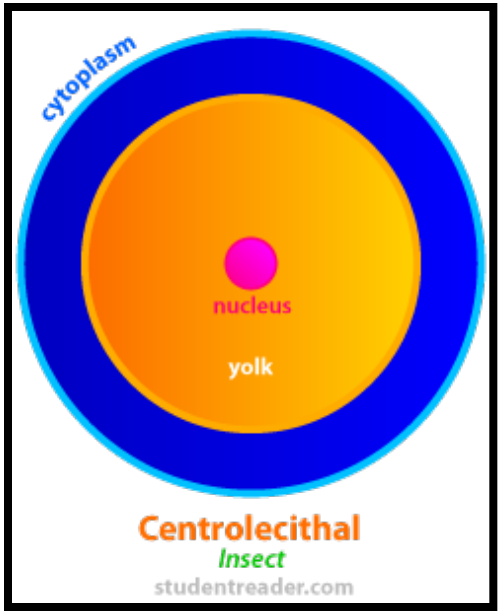
Eggs are classified by how much yolk is present

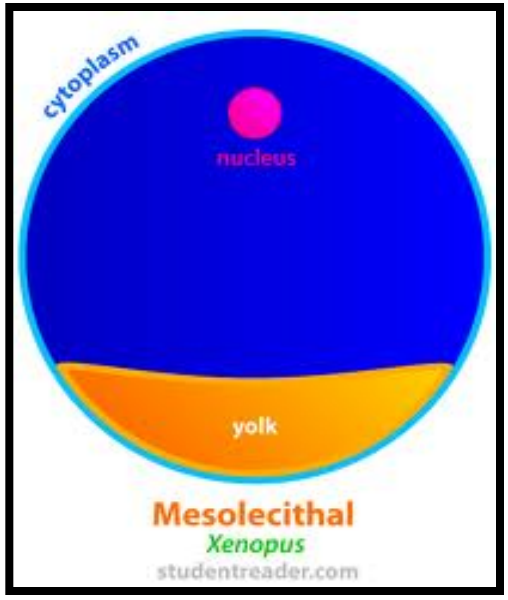
1. Alecithal eggs (a = without) little or none amount of yolk (placental mammals have alecithal eggs).
2. Isolecithal eggs (iso = equal) have a small amount of yolk that is equally distributed in the cytoplasm (sea urchins have isolecithal eggs).
3. Mesolecithal eggs (meso = middle) have a moderate amount of yolk, and the yolk is present mainly in the vegetal hemisphere (amphibians have mesolecithal eggs).
4. Telolecithal eggs (telo = end) have a large amount of yolk that fills the cytoplasm, except for a small area near the animal pole (fish, reptiles, and birds).
5. Centrolecithal eggs have a lot of yolk that is concentrated within the center of the cell (insects and arthropods).

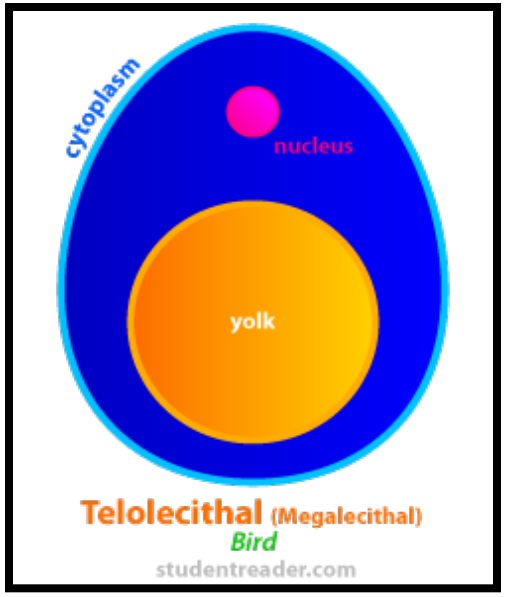
Eggs are classified by how much yolk is present

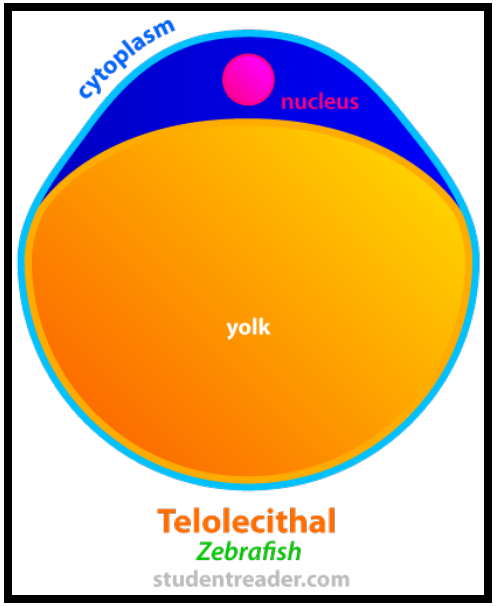












The pattern of cleavage of the zygote depends upon the pattern of yolk distribution

1. **Holoblastic cleavage: occurs in alecithal, isolecithal e mesolecithal eggs (mammals, sea urchins). The entire egg is cleaved during each division. Two types:**

    a. Equal Holoblastic (mammals, amnphioxus)

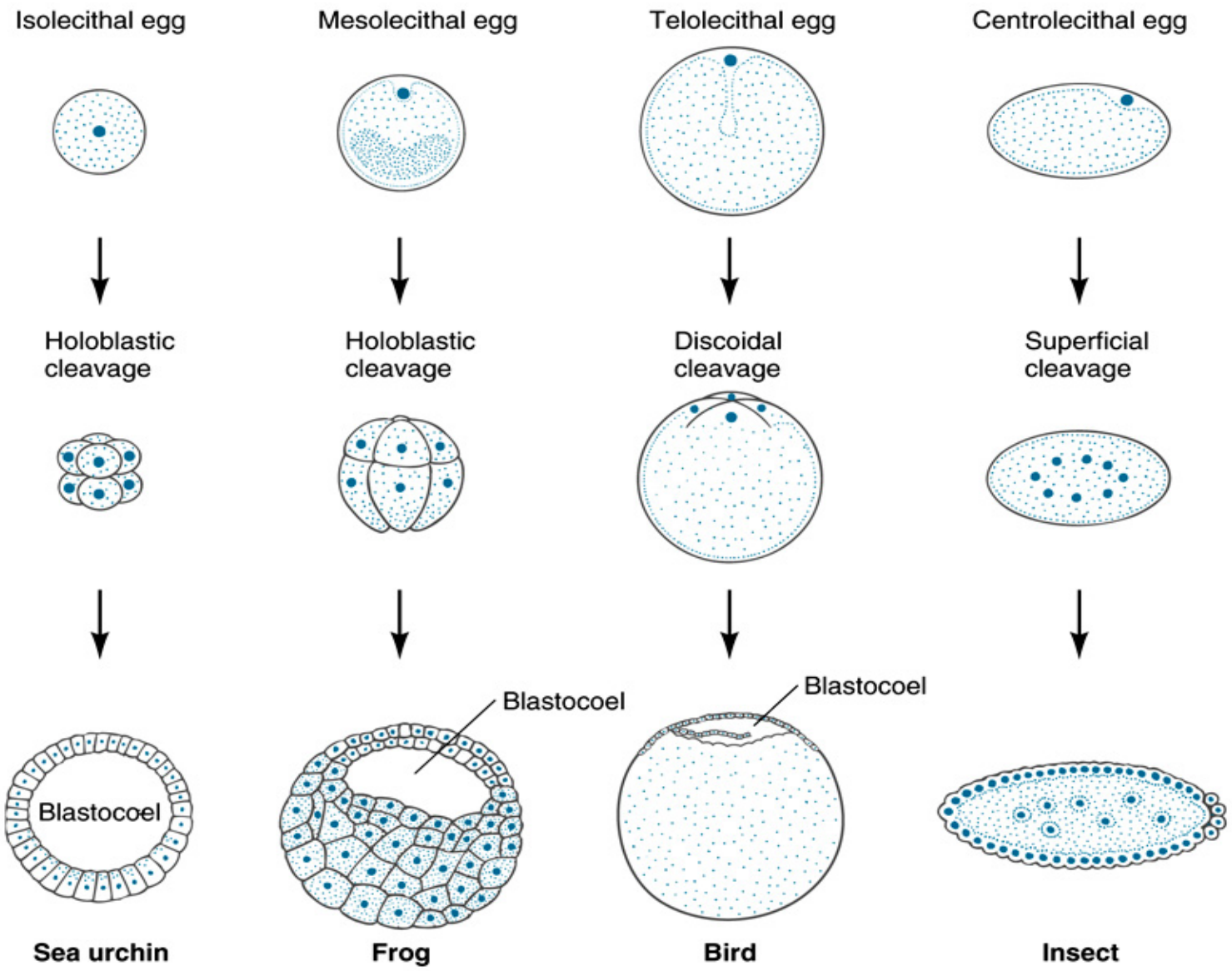
    b. Unequal Holoblastic (sea urchins, frogs)

1. **Meroblastic cleavage occurs when eggs have a lot of yolk. The egg does not divide completely at each division. Two types:**

    a. **Discoidal cleavage is limited to a small disc of cytoplasm at the animal pole. All of the yolk filled cytoplasm fails to cleave (characteristic of telolecithal eggs such as birds).**

    b. **Superficial cleavage is limited to a thin surface area of cytoplasm that covers the entire egg. The inside of the egg that is filled with yolk fails to cleave (centrolecithal eggs such as insects).**

Typical cleavage patterns of isolecithal, mesolecithal, telolecithal and centrolecithal eggs



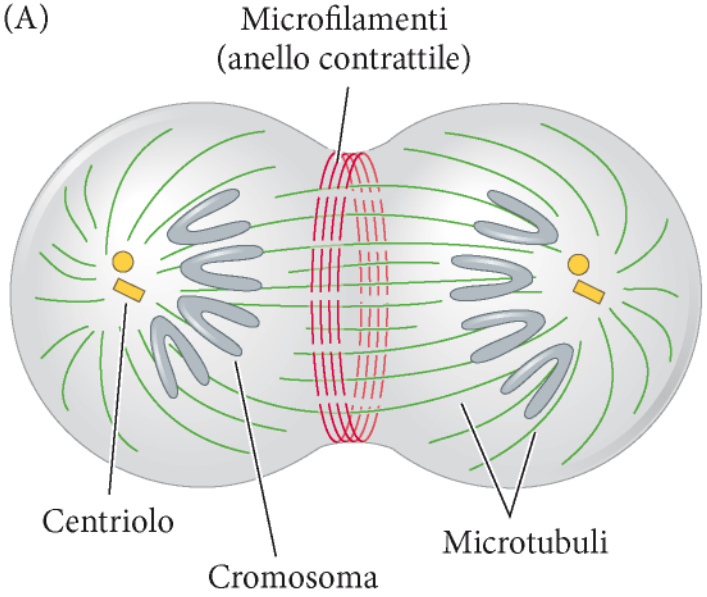
Typical cleavage patterns of isolecithal, mesolecithal, telolecithal and centrolecithal eggs

Tabella 5.1 **Tipi di uova, modalità di segmentazione e modelli rappresentativi**

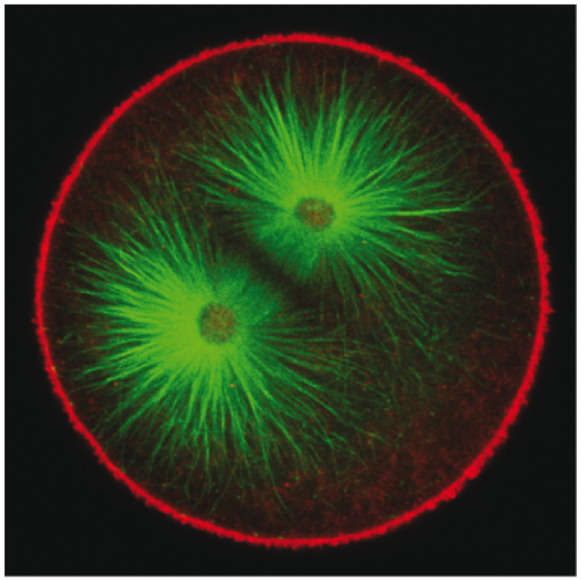
Tipo di uovo	Tipo di segmentazione	Modello di segmentazione	Forma blastula	Gruppo animale
Isolecitico (poco vitello uniformemente distribuito)	Oloblastica (l'uovo si divide totalmente)	Radiale, bilaterale, spirale, rotazionale	Sferica (un singolo strato di blastomeri delimita il blastocele)	Echinodermi, cefalocordati, ascidie, molluschi, anellidi, mammiferi euteri
Mesolecitico (moderata quantità di vitello, più abbondante nell'emisfero vegetativo)	Oloblastica	Radiale	Sferica (più strati di blastomeri delimitano il blastocele eccentrico)	Anfibi e alcuni pesci
Telolecitico (l'uovo è quasi totalmente ripieno di vitello, tranne al polo animale in corrispondenza del blastodisco)	Meroblastica (l'uovo non si segmenta totalmente)	Discoidale (i blastomeri formano un disco che poggia sul vitello insegmentato)	Disco cellulare (formato da epiblasto e ipoblasto, separati da un blastocele)	Molti pesci, uccelli e rettili
Centrolecitico (il vitello è concentrato al centro dell'uovo)	Meroblastica	Superficiale (i blastomeri si formano sulla superficie dell'uovo)	Ovoidale (i blastomeri formano un singolo strato, detto blastoderma, che circonda il vitello)	Insetti e altri artropodi

Secondo B. M. Carlson (1988)

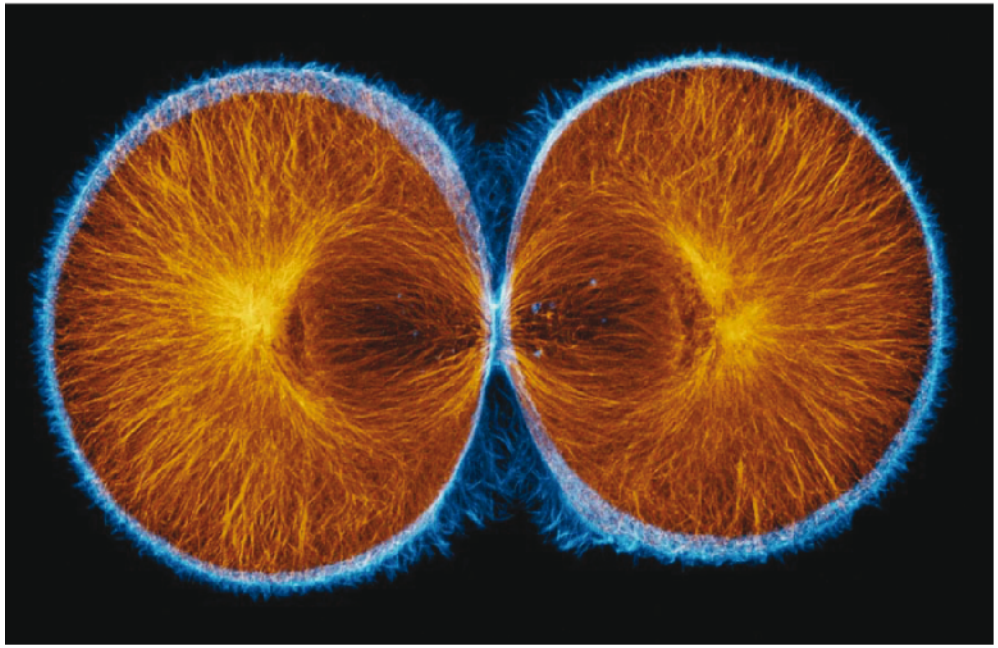
(A)


Microfilamenti
(anello contrattile)
Centriolo
Cromosoma
Microtubuli

(B)



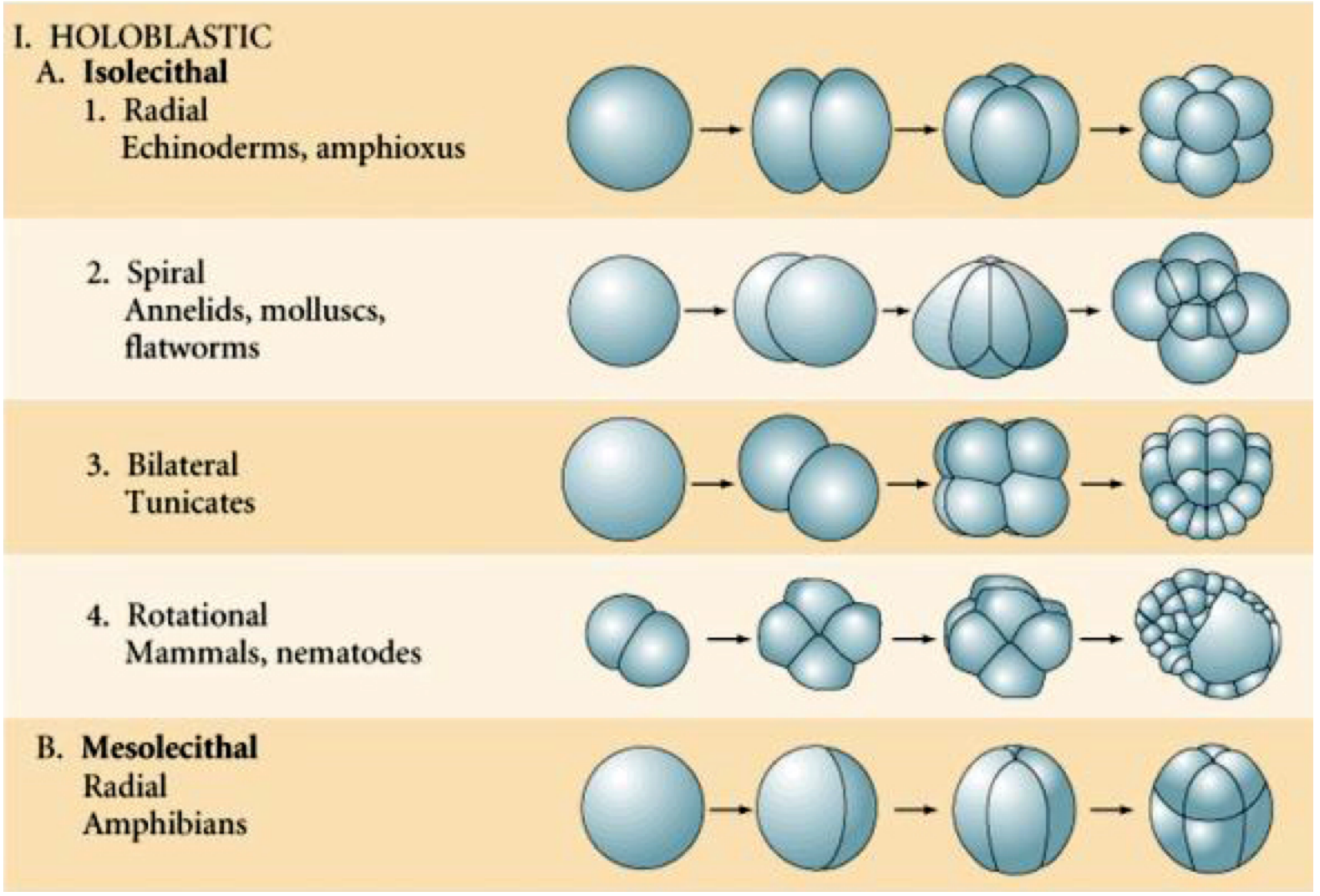
(C)



Quindi in base al tipo di uovo vi sono due grosse modalità di segmentazione:
TOTALE o OLOBLASTICA,
PARZIALE o MEROBLASTICA

La segmentazione è influenzata dalla presenza del vitello che rallenta od ostacola la formazione del solco di divisione

Quindi in base al tipo di uovo vi sono due grosse modalità di segmentazione: TOTALE o OLOBLASTICA - PARZIALE o MEROBLASTICA



SEGMENTAZIONE OLOBLASTICA RADIALE

Con blastomeri uguali

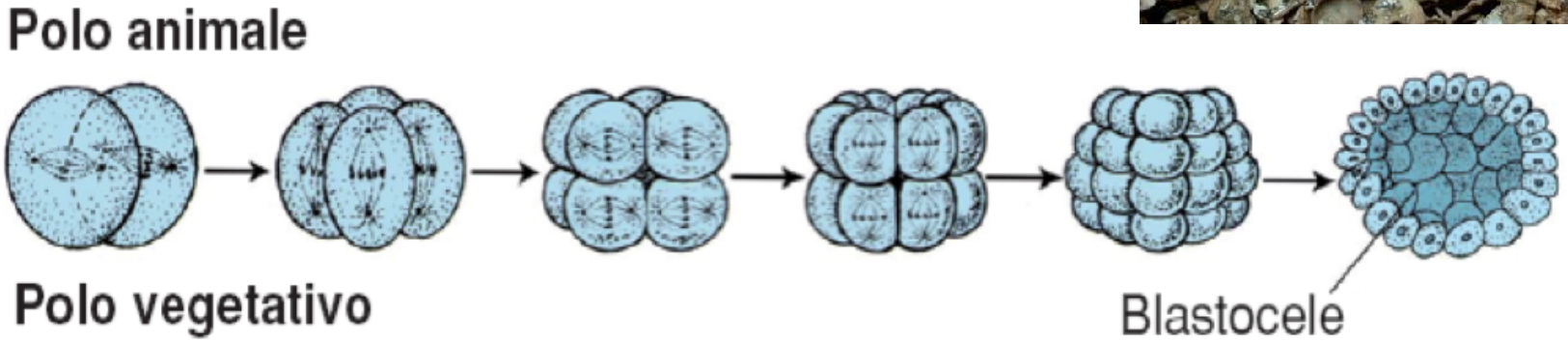
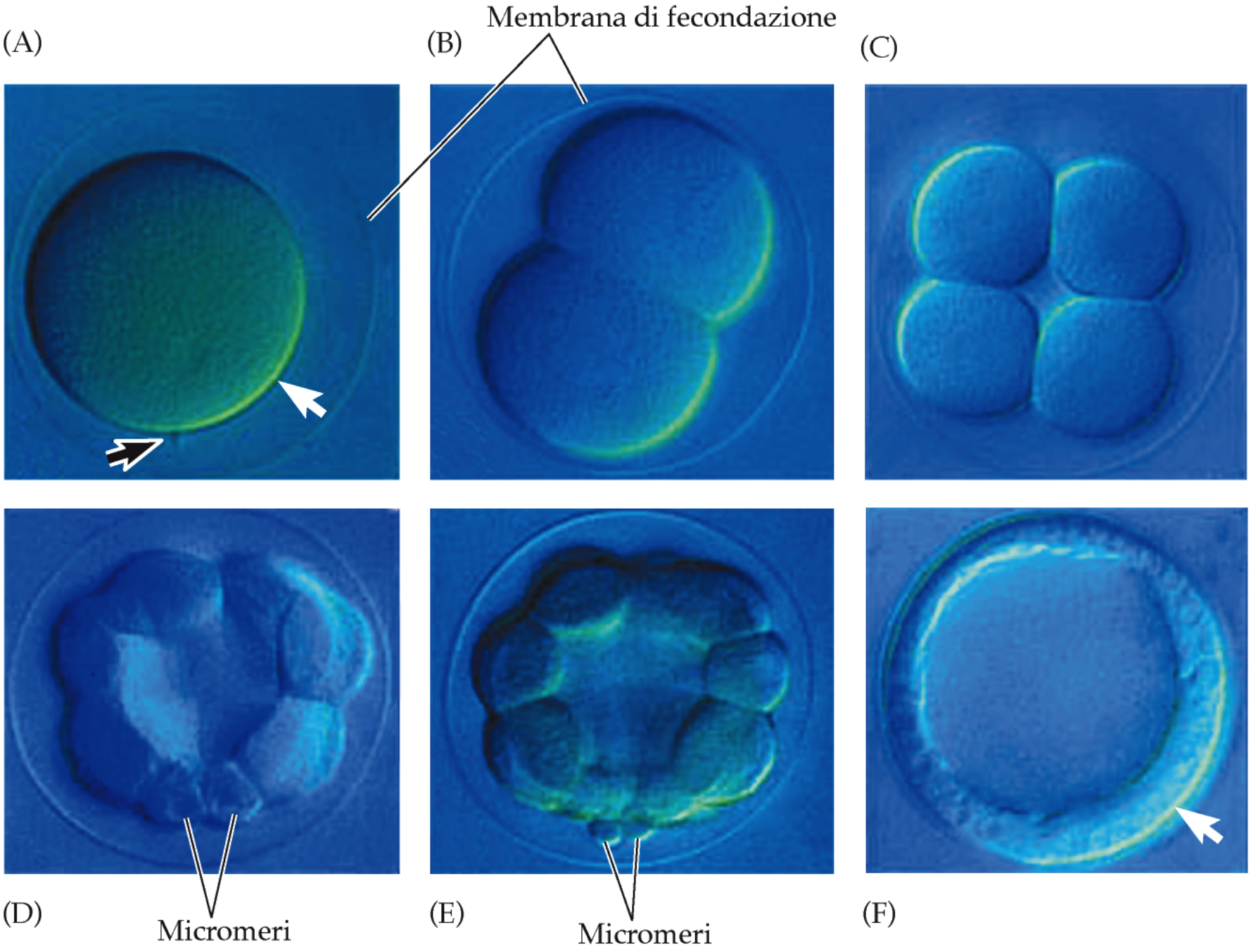


Figura 5.5 **Segmentazione oloblastica radiale di uovo di anfiosso dallo stadio a due blastomeri sino allo stadio di blastula.** La blastula è vista in sezione saggitale dal polo animale al polo vegetativo. Nella figura non sono indicate le semilune.


(A)
(B)
Membrana di fecondazione
(C)
(D)
Micromeri
(E)
Micromeri
(F)

SEGMENTAZIONE OLOBLASTICA RADIALE

Con blastomeri uguali solo nelle prime 3 divisioni

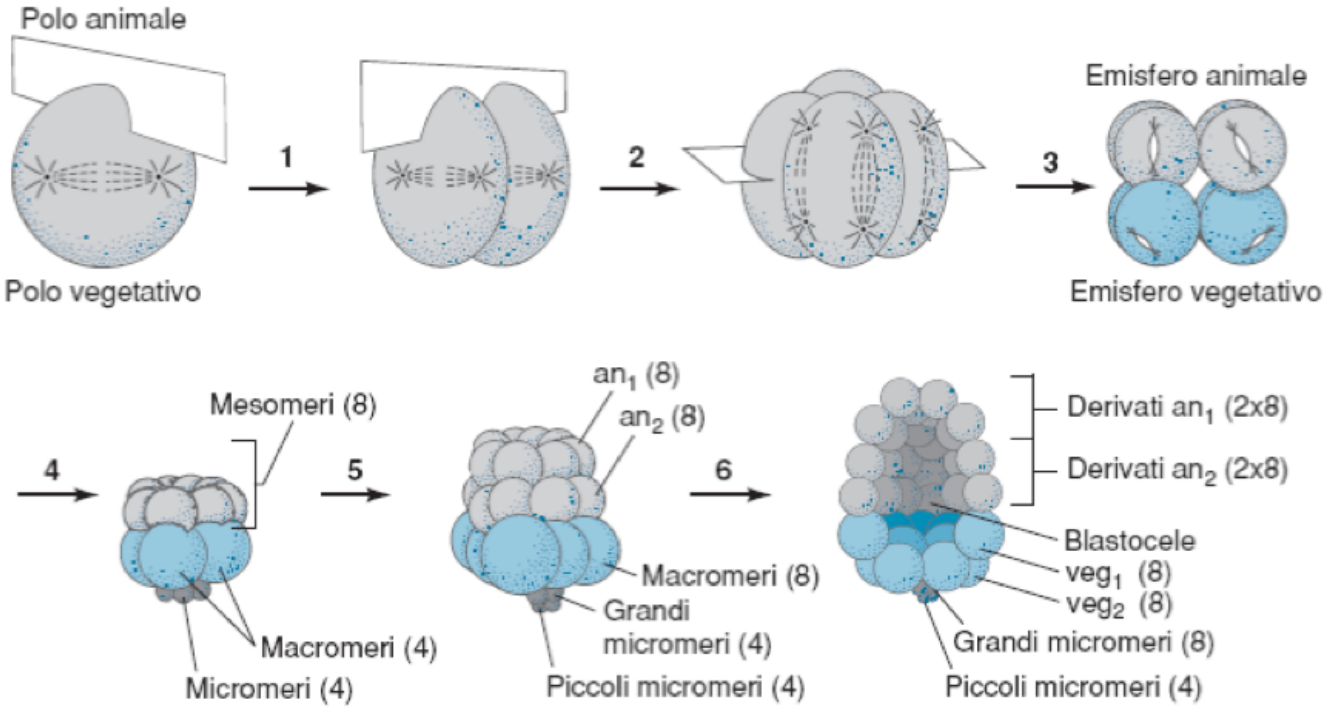
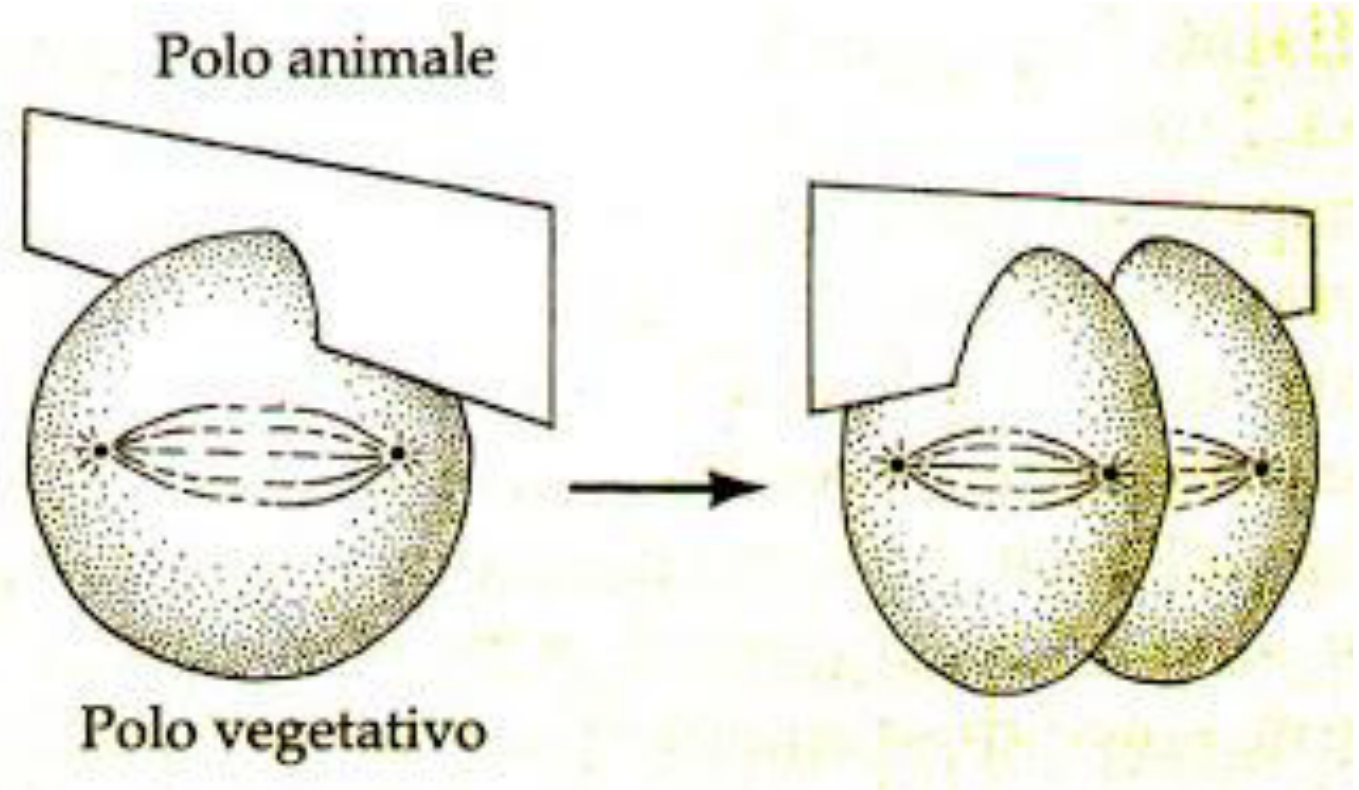
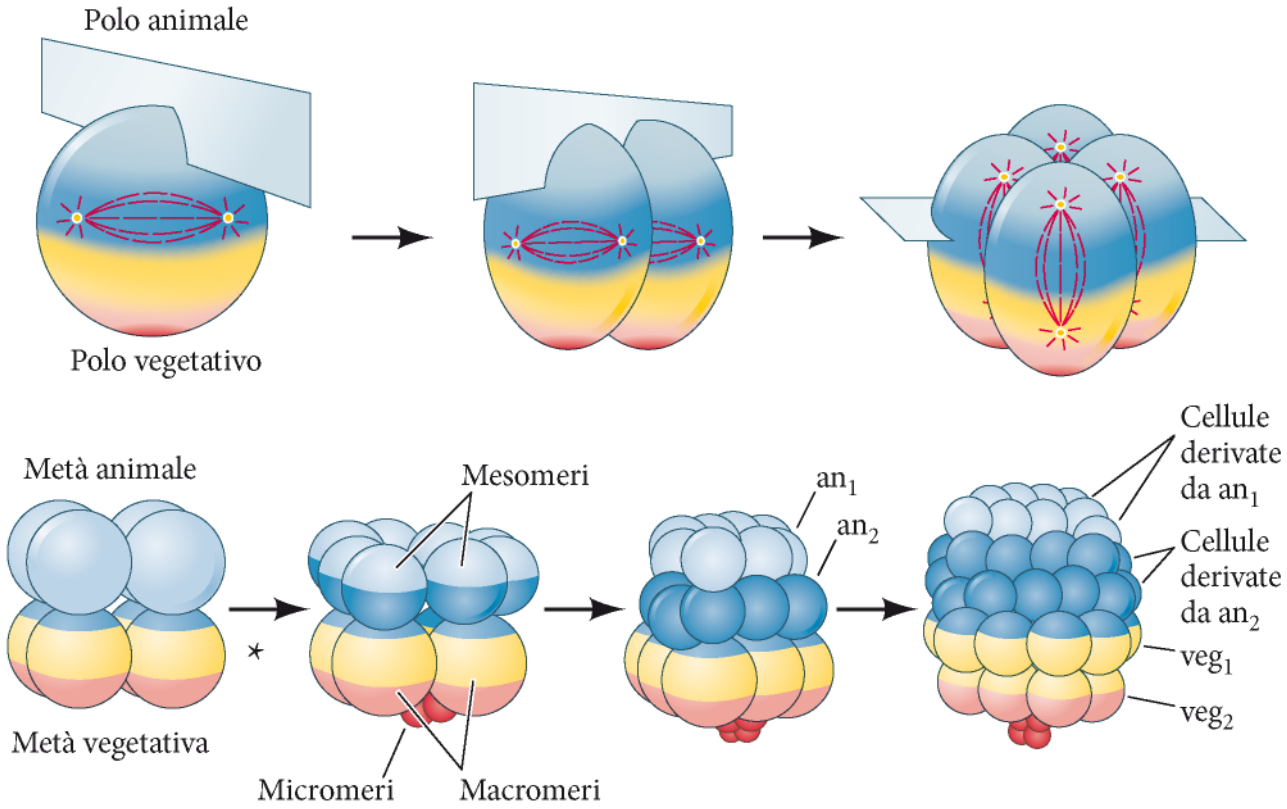


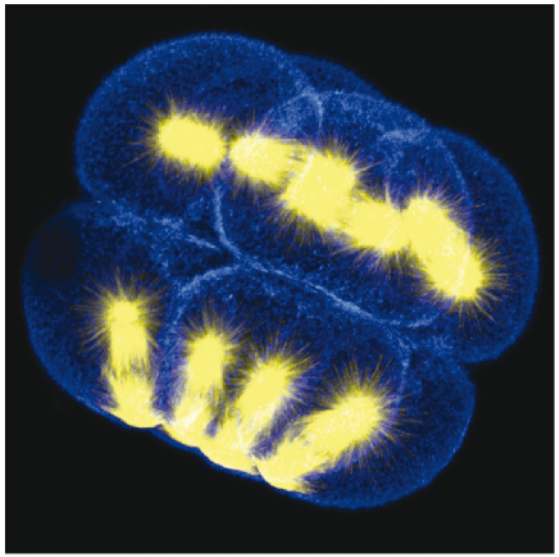
Figura 5.4 Segmentazione dell'uovo di riccio di mare. Il primo e il secondo piano di segmentazione sono meridiani e passano attraverso l'asse animale-vegetativo. Il terzo piano di divisione è equatoriale e perpendicolare all'asse animale-vegetativo. Con la quarta divisione di segmentazione i blastomeri animali si dividono in modo uguale secondo un piano meridiano formando otto mesomeri mentre i blastomeri vegetativi si dividono in modo diseguale formando quattro macromeri e quattro micromeri al polo vegetativo. Con la quinta divisione di segmentazione si formano due file animali (an_1 e an_2) di otto mesomeri ciascuna, una fila di blastomeri vegetativi di otto macromeri, quattro grandi micromeri e quattro piccoli micromeri. Alla sesta divisione di segmentazione l'embrione è mostrato in sezione polo animale /polo vegetativo. Si evidenzia il blastocele, in posizione centrale; inoltre nell'emisfero animale si riscontrano due file di mesomeri di otto cellule ciascuna (an_1) che sormontano altre due file di mesomeri di otto cellule ciascuna (an_2); nell' emisfero vitellino vi sono due file di macromeri (veg_1 e veg_2) di otto cellule ciascuna, otto grandi micromeri e infine, all'estremo polo vitellino, 4 piccoli micromeri. Questi ultimi non si dividono durante la sesta divisione di segmentazione.


Polo animale
Polo vegetativo

(A)

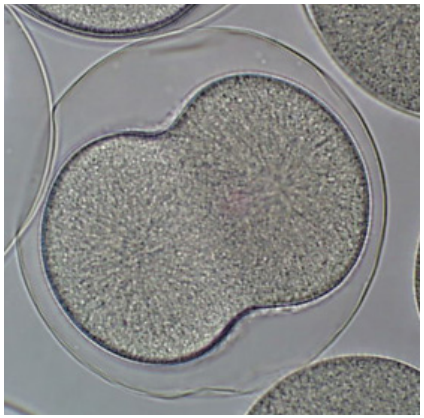

Polo animale
Polo vegetativo
Metà animale
Metà vegetativa
Mesomeri
Micromeri
Macromeri
an1
an2
Cellule derivate da an1
Cellule derivate da an2
veg1
veg2

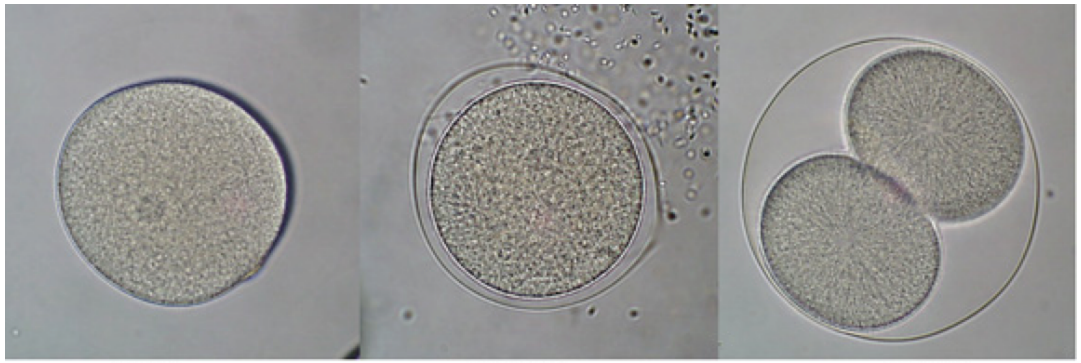
(B)

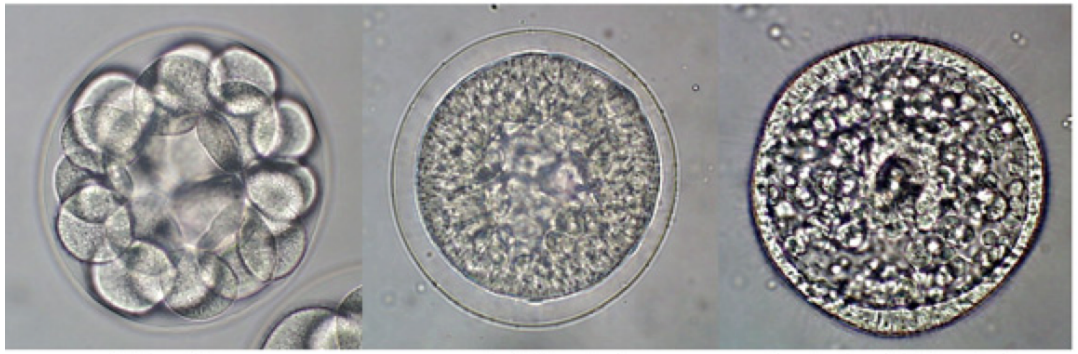


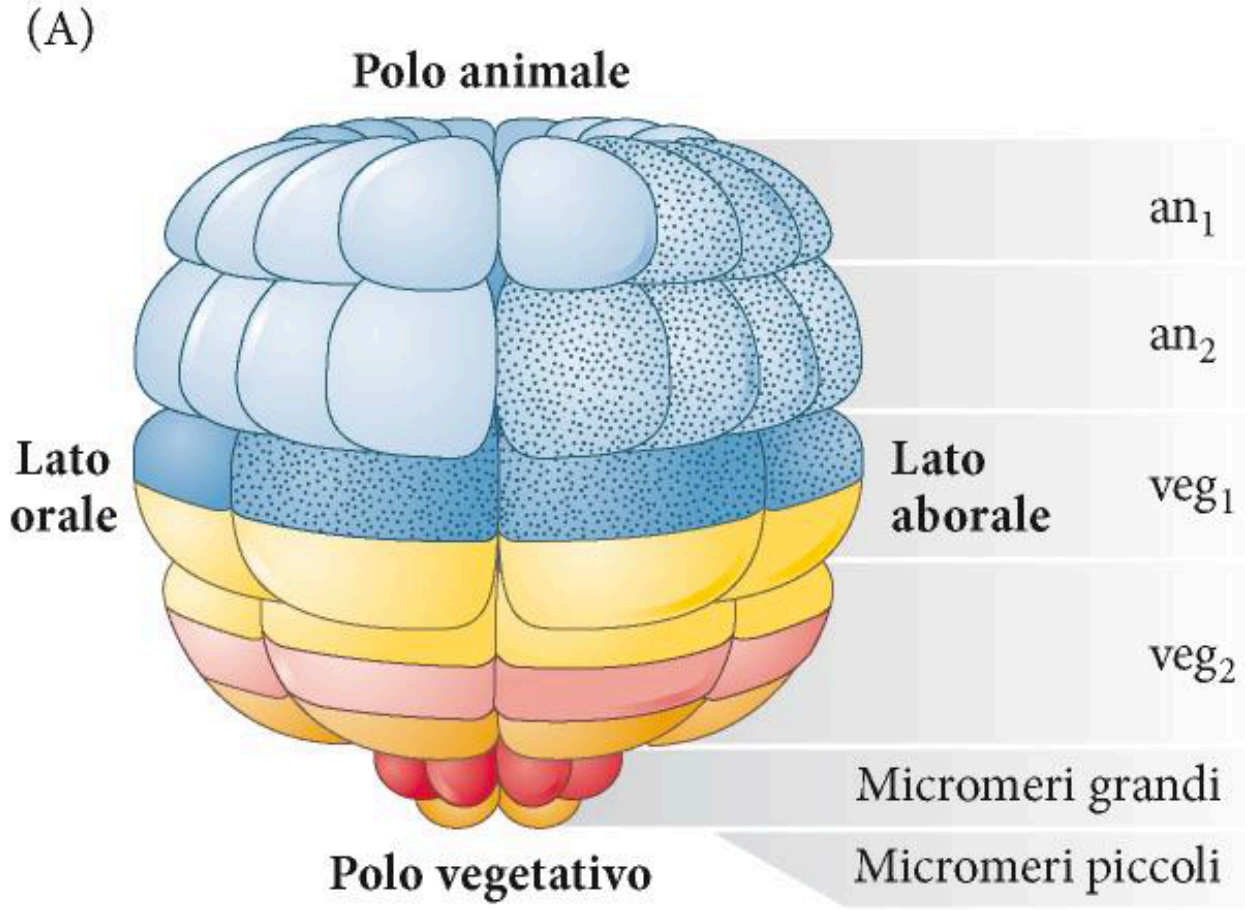
SEGMENTAZIONE OLOBLASTICA RADIALE

In riccio di mare

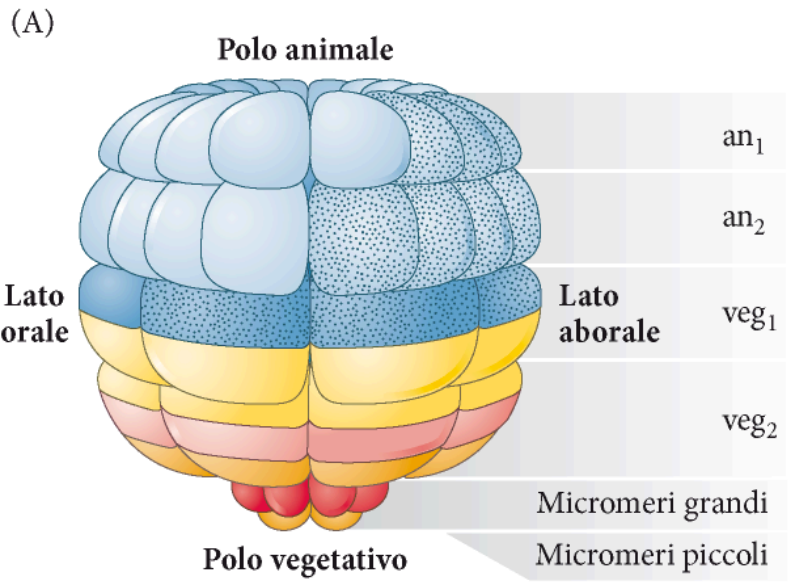


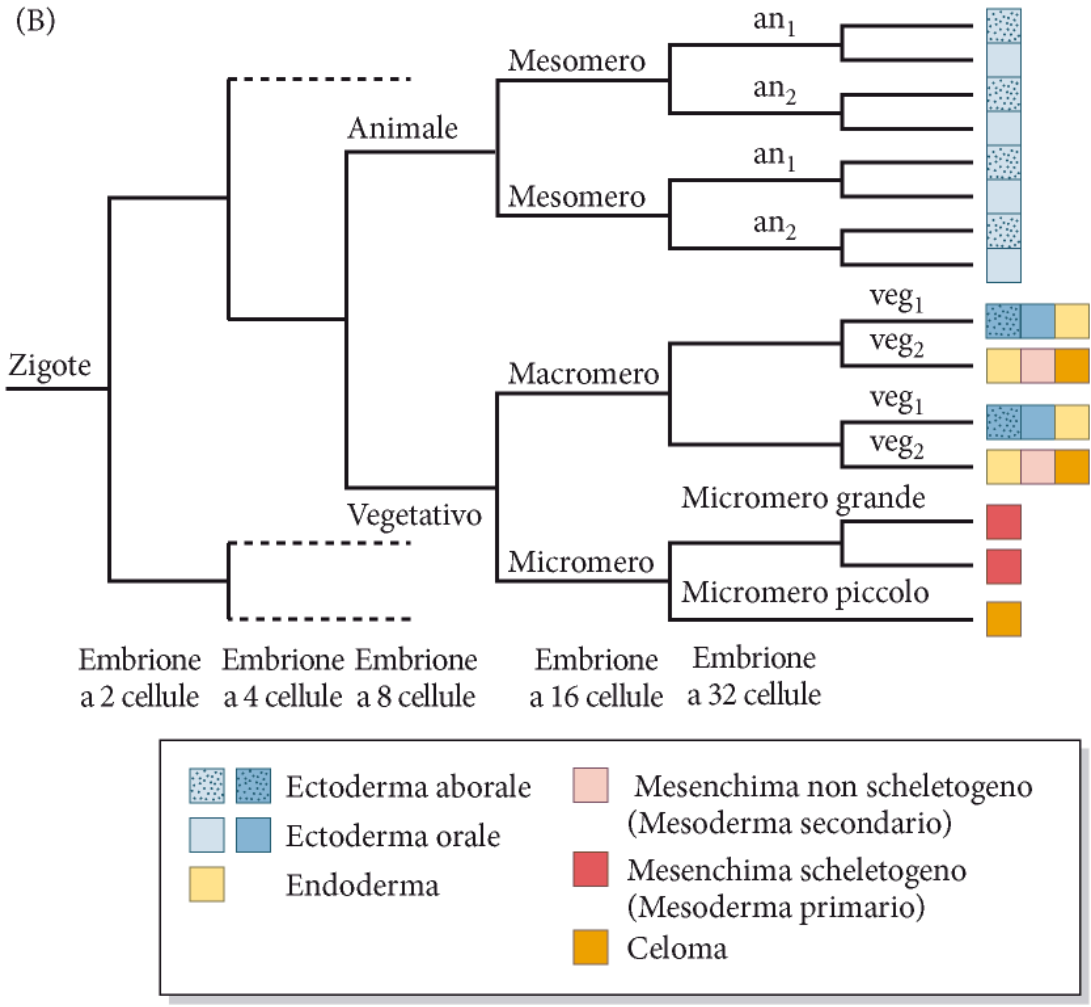


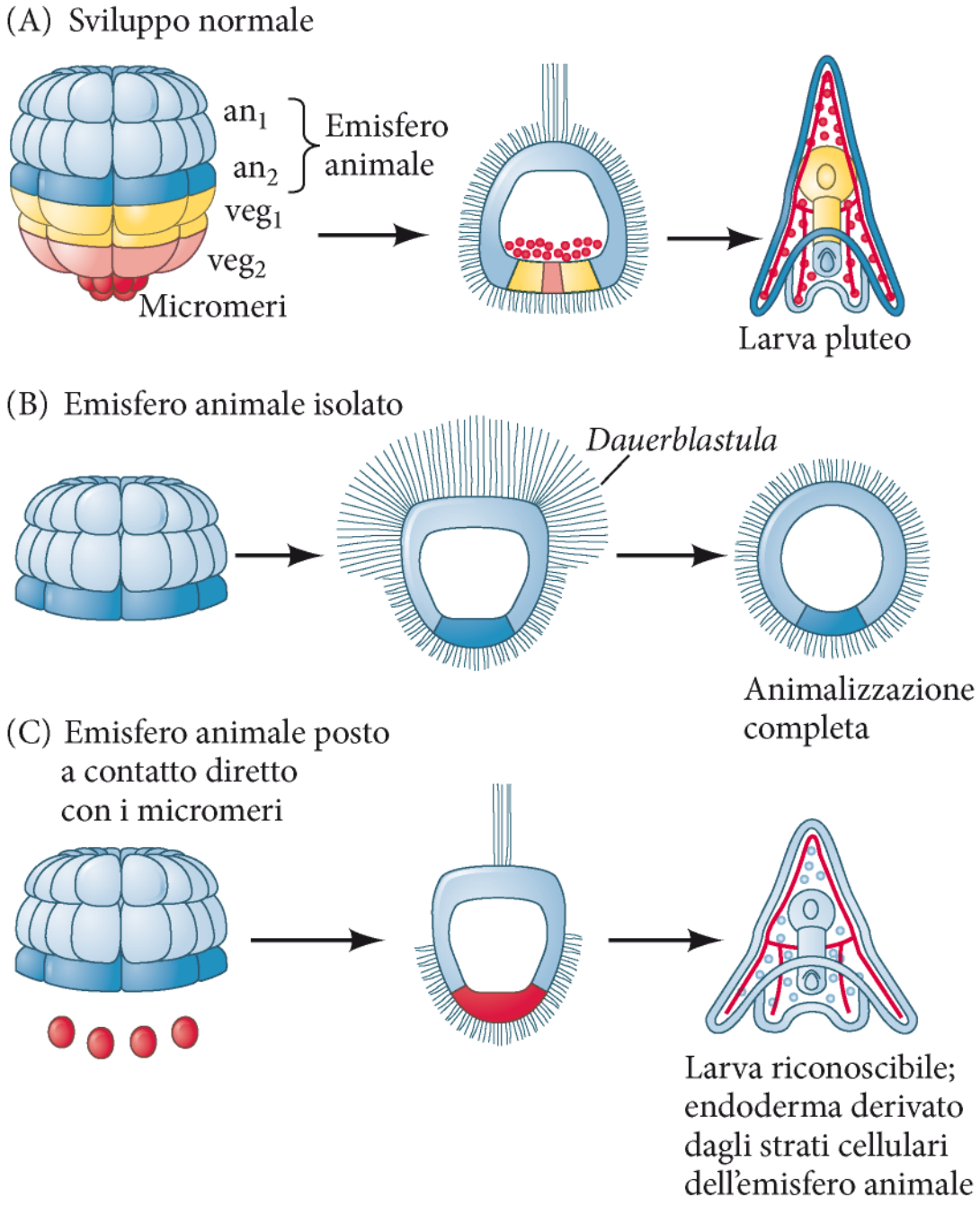




Una mappa presuntiva è una mappa che illustra la discendenza di linee cellulari provenienti da regioni specifiche dell'embrione. Una mappa che rappresenta ciòche sarà su una struttura che deve ancora dar luogo a questi organi.

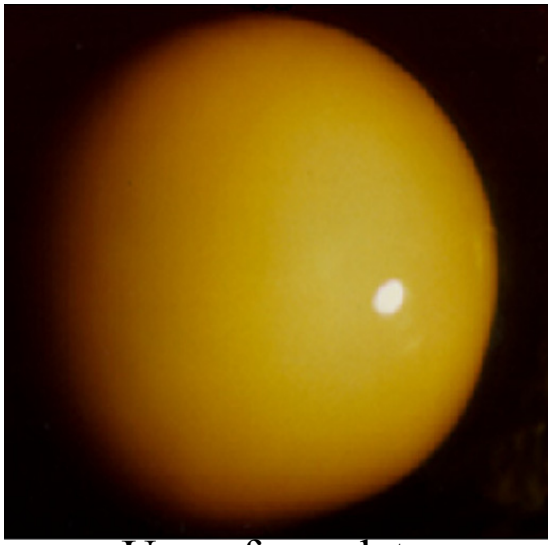

(A)
Polo animale
an1
an2
Lato orale
Lato aborale
veg1
veg2
Micromeri grandi
Micromeri piccoli
Polo vegetativo


(B)
an1
Mesomero
an2
Animale
an1
Mesomero
an2
veg1
Zigote
veg2
Macromero
veg1
veg2
Micromero grande
Vegetativo
Micromero
Micromero piccolo
Embrione a 2 cellule
Embrione a 4 cellule
Embrione a 8 cellule
Embrione a 16 cellule
Embrione a 32 cellule
Ectoderma aborale
Ectoderma orale
Endoderma
Mesenchima non scheletogeno (Mesoderma secondario)
Mesenchima scheletogeno (Mesoderma primario)
Celoma

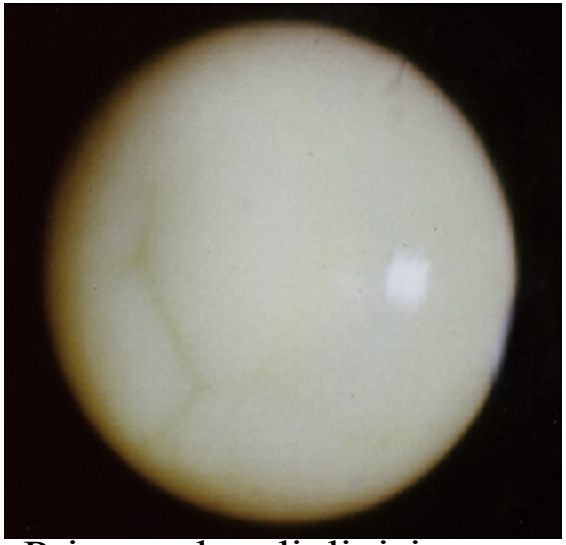

(A) Sviluppo normale
an1
an2
Emisfero animale
veg1
veg2
Micromeri
Larva pluteo
(B) Emisfero animale isolato
Dauerblastula
Animalizzazione completa
(C) Emisfero animale posto a contatto diretto con i micromeri
Larva riconoscibile; endoderma derivato dagli strati cellulari dell'emisfero animale

SEGMENTAZIONE OLOBLASTICA RADIALE

In Anfibio



Uovo fecondato
(1 giorno)



Primo solco di divisione
(1 giorno)

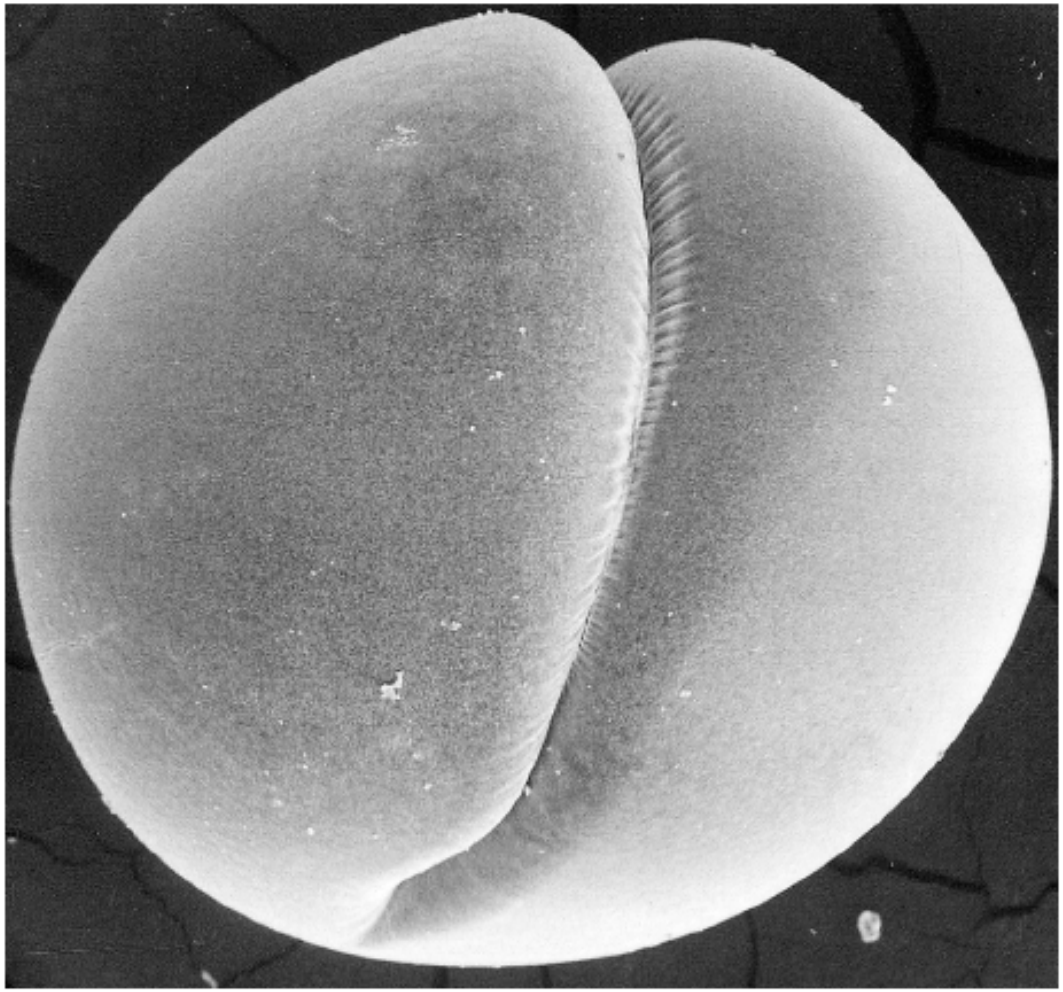
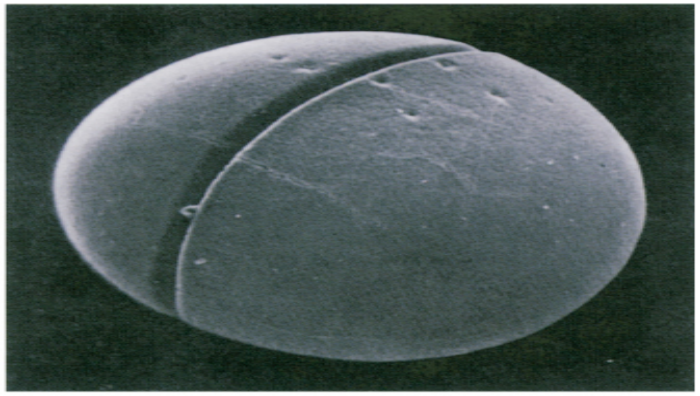
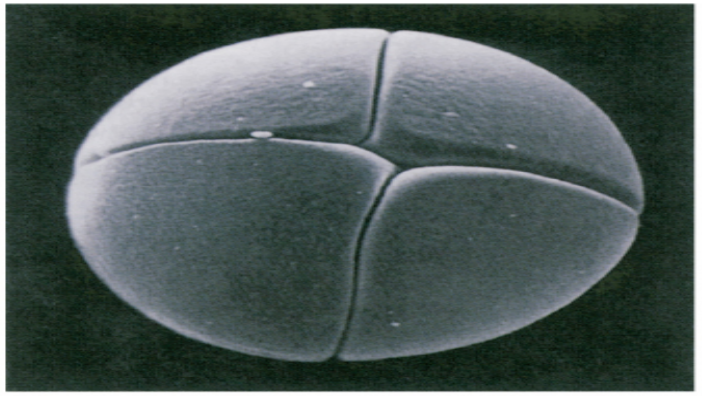


Figura 5.1 Embrione di rana durante la prima divisione di segmentazione visto al microscopio elettronico a scansione. Il

Fig. 8.2: *Microfotografie di embrioni di Xenopus in corso di segmentazione (gli embrioni sono privi di strato gelatinoso e di membrana di fecondazione, × 50)*



Stadio a 2 cellule

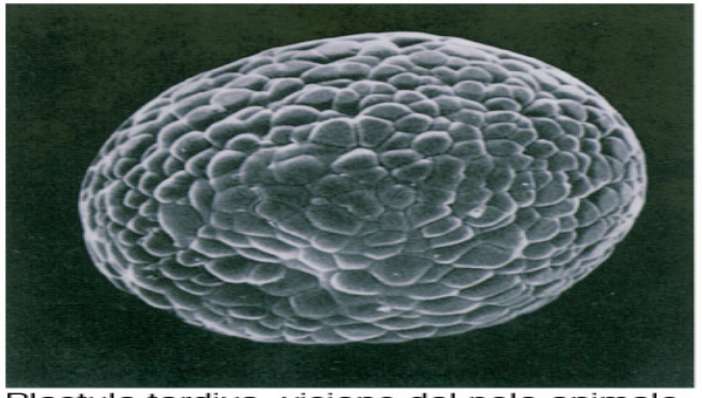


Stadio a 4 cellule

Stadio a 16 cellule, visione dal polo animale

Stadio a 16 cellule, visione dal polo vegetativo

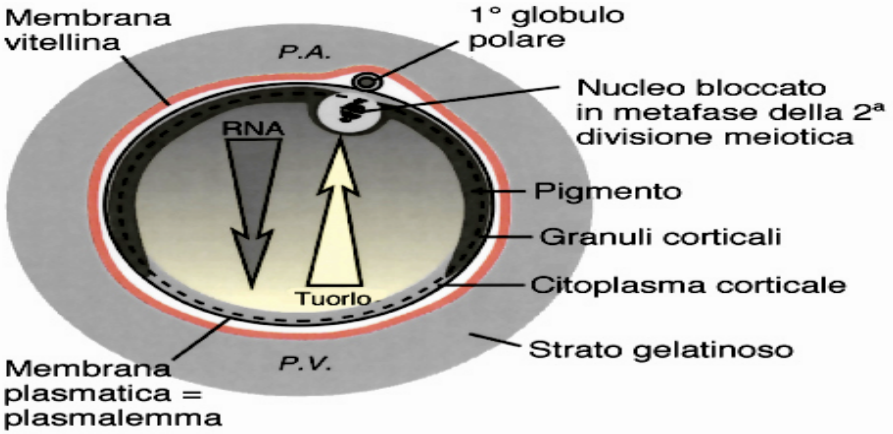
Stadio a 32 cellule in formazione



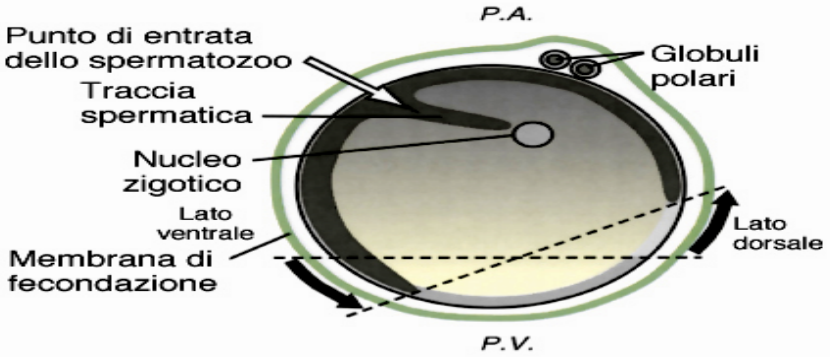
Blastula tardiva, visione dal polo animale

Fig. 8.1: ***L'uovo e le prime tappe della segmentazione***

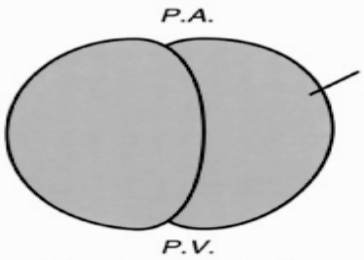
a) L'uovo maturo non fecondato



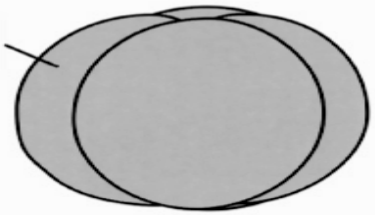
b) Rotazione di simmetrizzazione
(l'uovo è rappresentato senza strato gelatinoso)



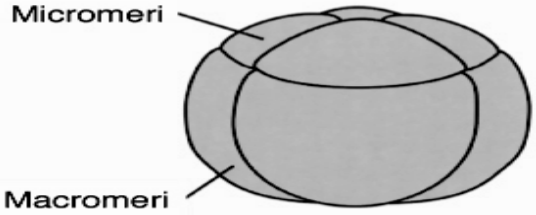
c) La segmentazione vista dall'esterno
(lo strato gelatinoso, la membrana di fecondazione e i globuli polari non sono rappresentati)



Stadio a 2 cellule

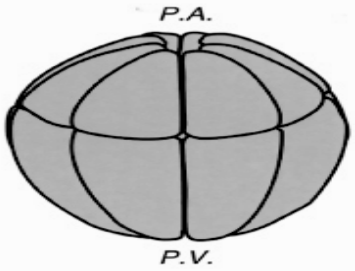


Stadio a 4 cellule

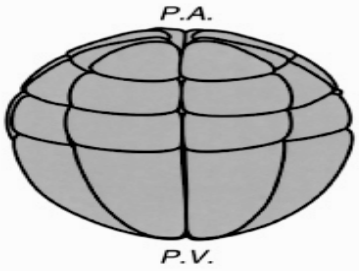


Stadio a 8 cellule

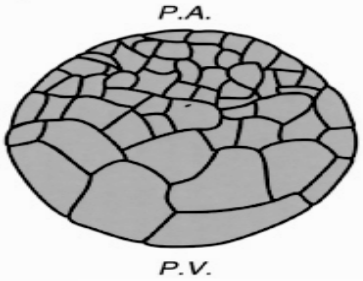
d) Blastula



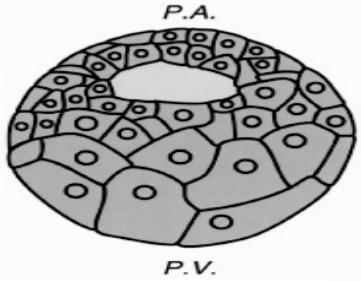
Stadio a 16 cellule



Stadio a 32 cellule



Veduta esterna

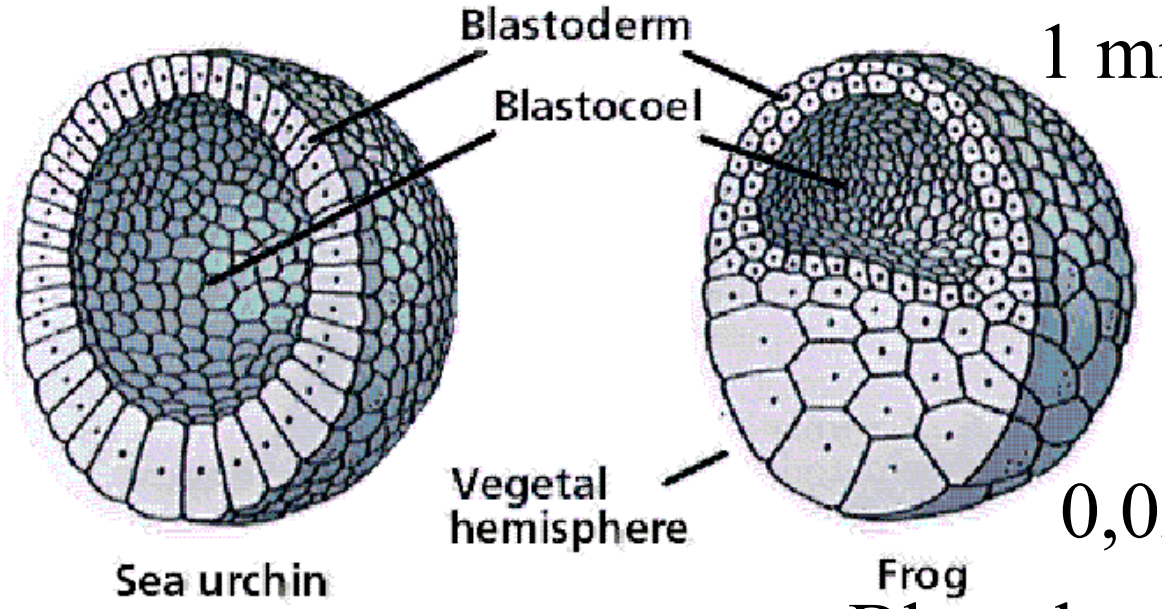


Sezione meridiana

https://www.youtube.com/watch?v=EQkYEHr8a8s

https://www.youtube.com/watch?v=IjyemX7C_8U

Blastula di riccio di mare e rana



1 mm al min.

0,02 mm al min.

Blastula: 128 blastomeri

Funzione del blastocele:

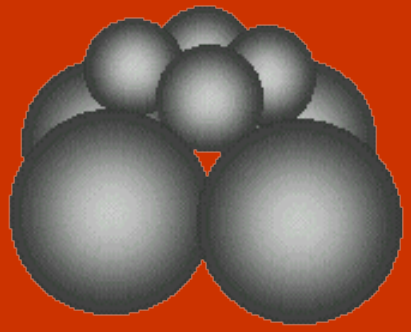
• Consente la migrazione durante la gastrulazione

• Impedisce alle cellule del polo vegetative (futuro endoderma) di prendere contatto con quelle dell´emisfero animale (ectoderma, epidermide e tessuto nervoso)

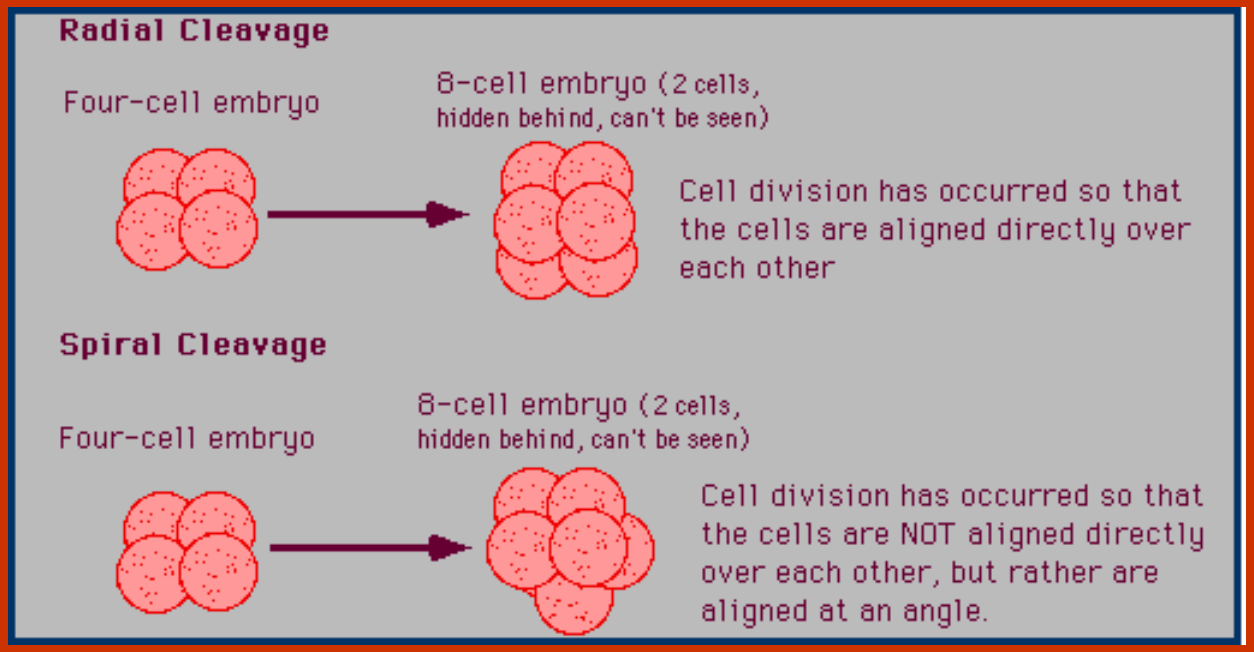
https://www.youtube.com/watch?v=R1x4iBL-02s

Primi piani di segmentazione radiale e spirale

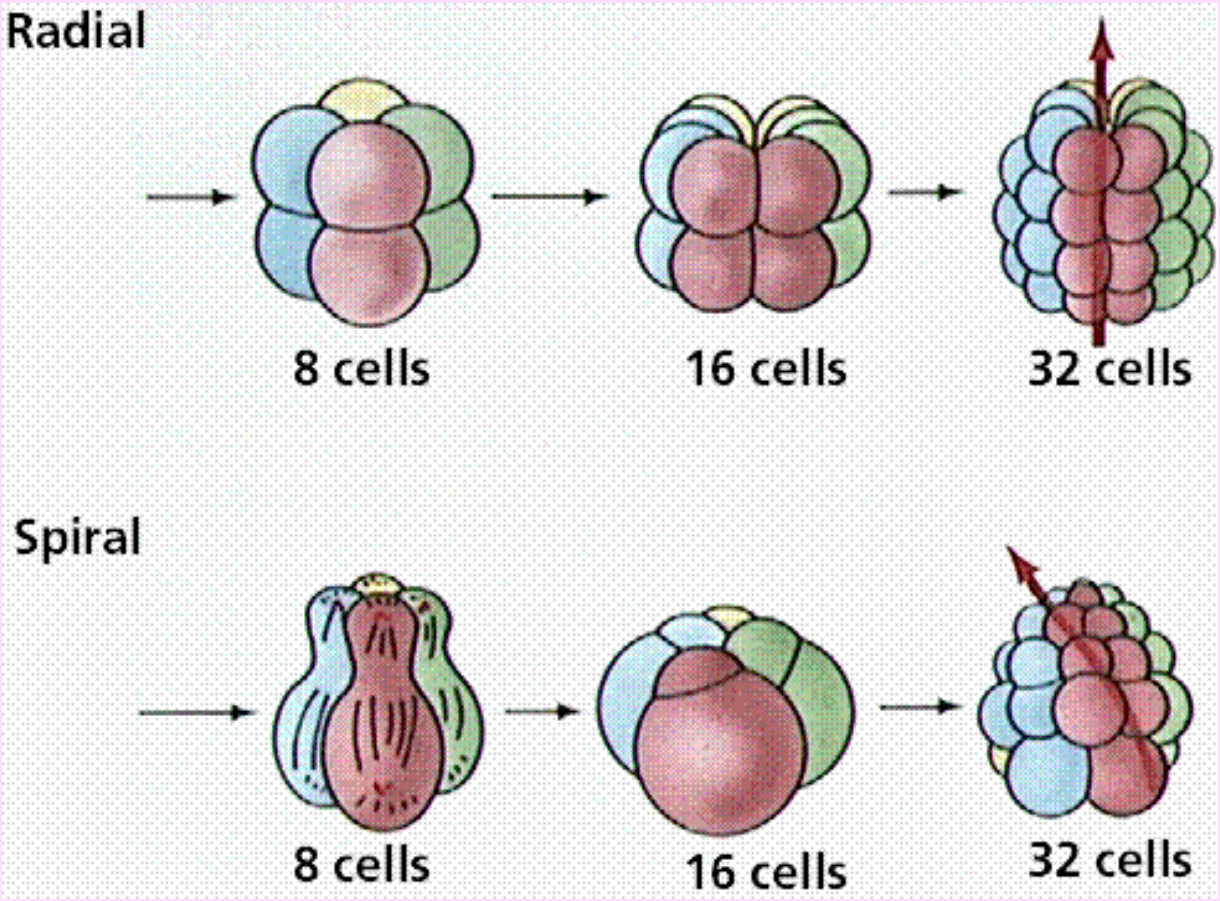
Radial Cleavage

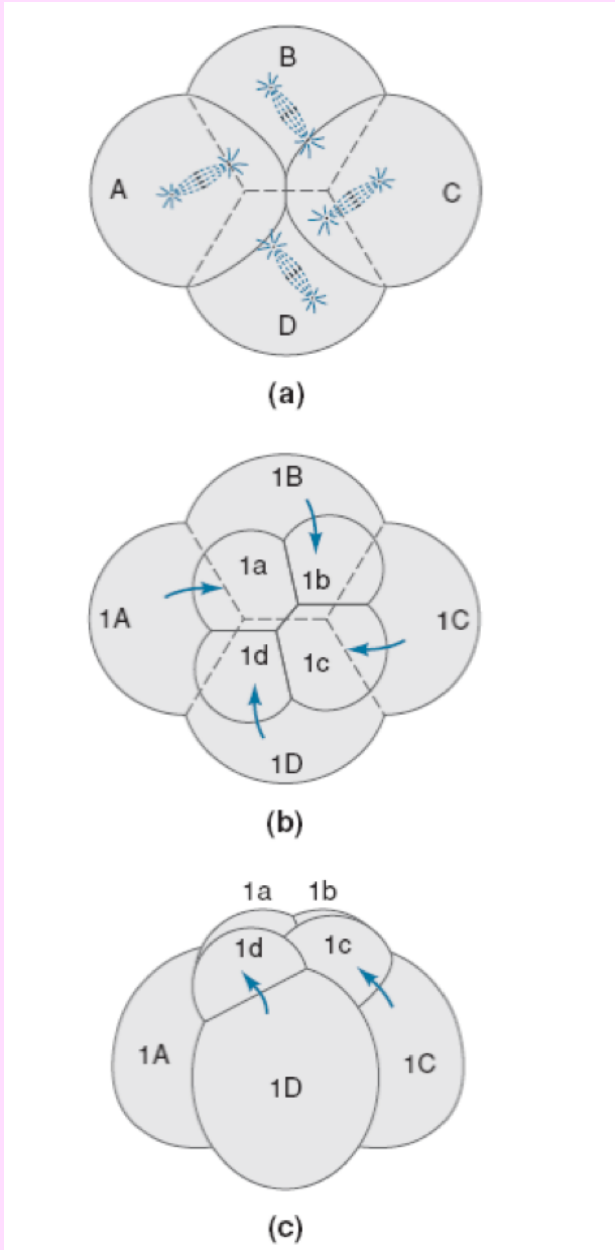


Spiral Cleavage

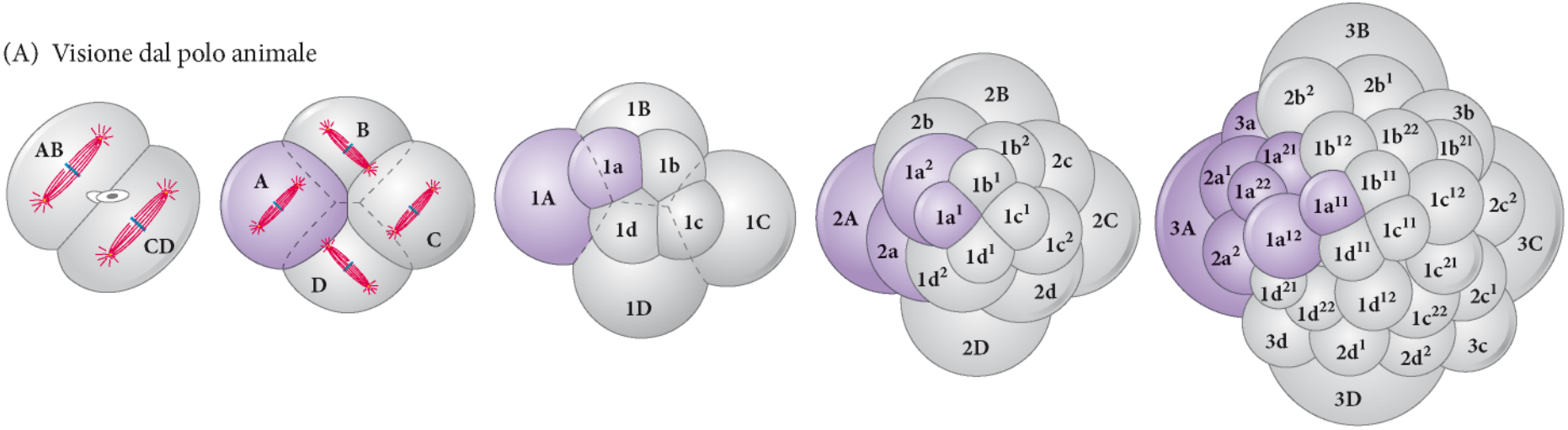


Segmentazione radiale e spirale

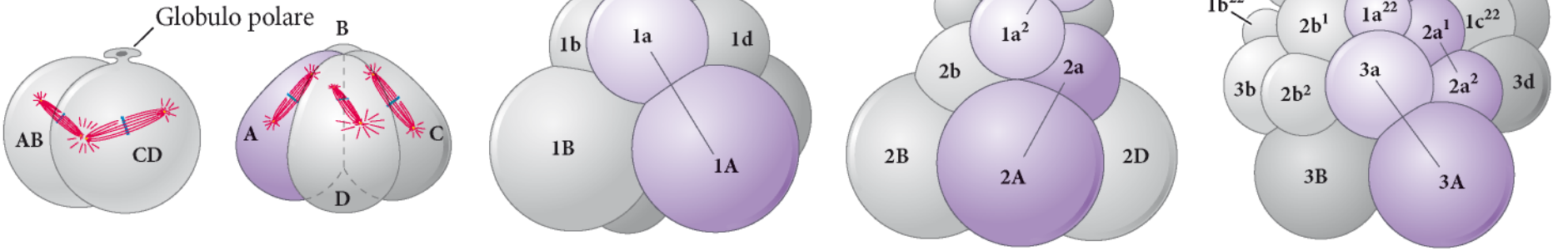




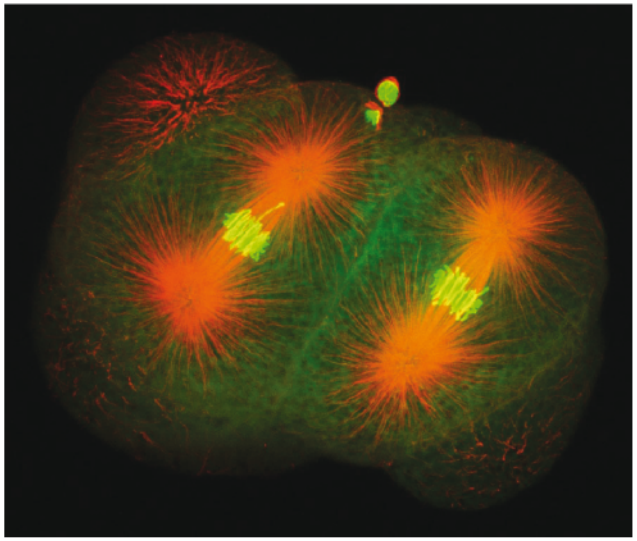
(A) Visione dal polo animale



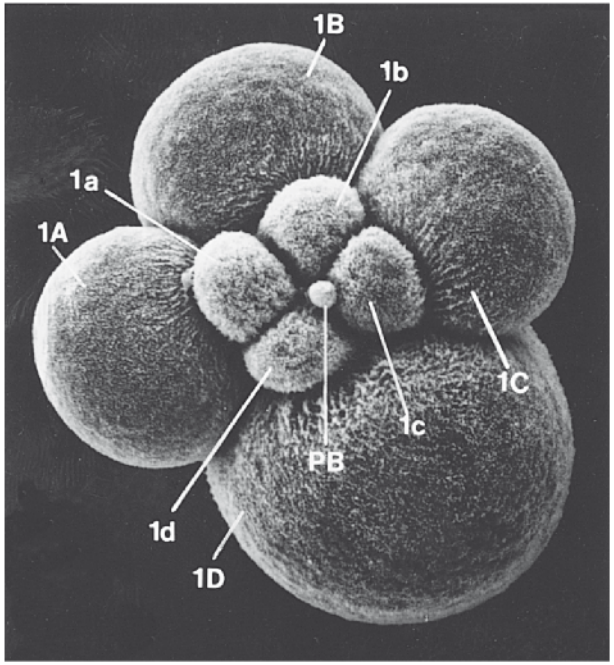
(B) Visione laterale



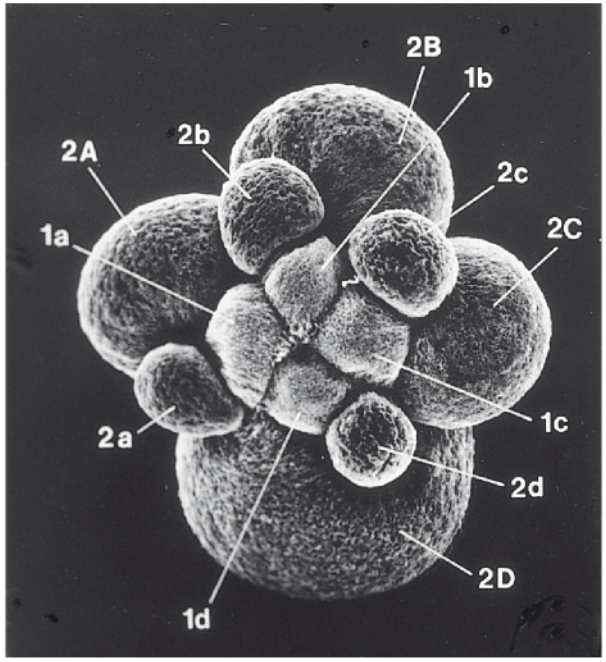
(A)



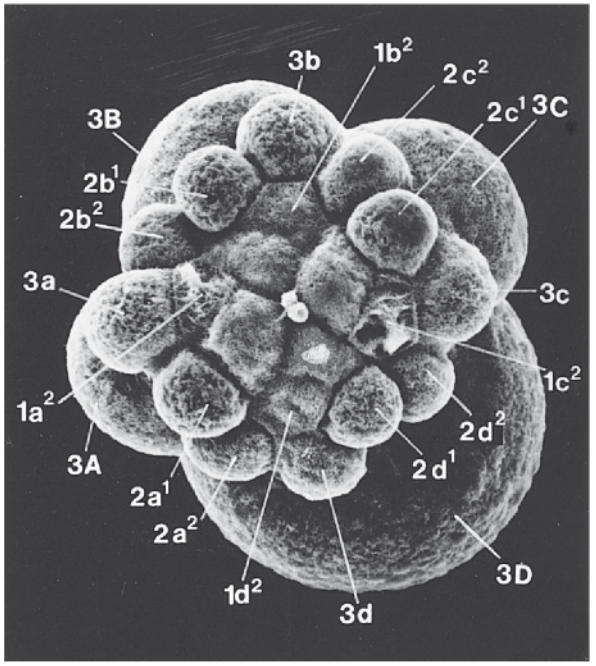
(B)

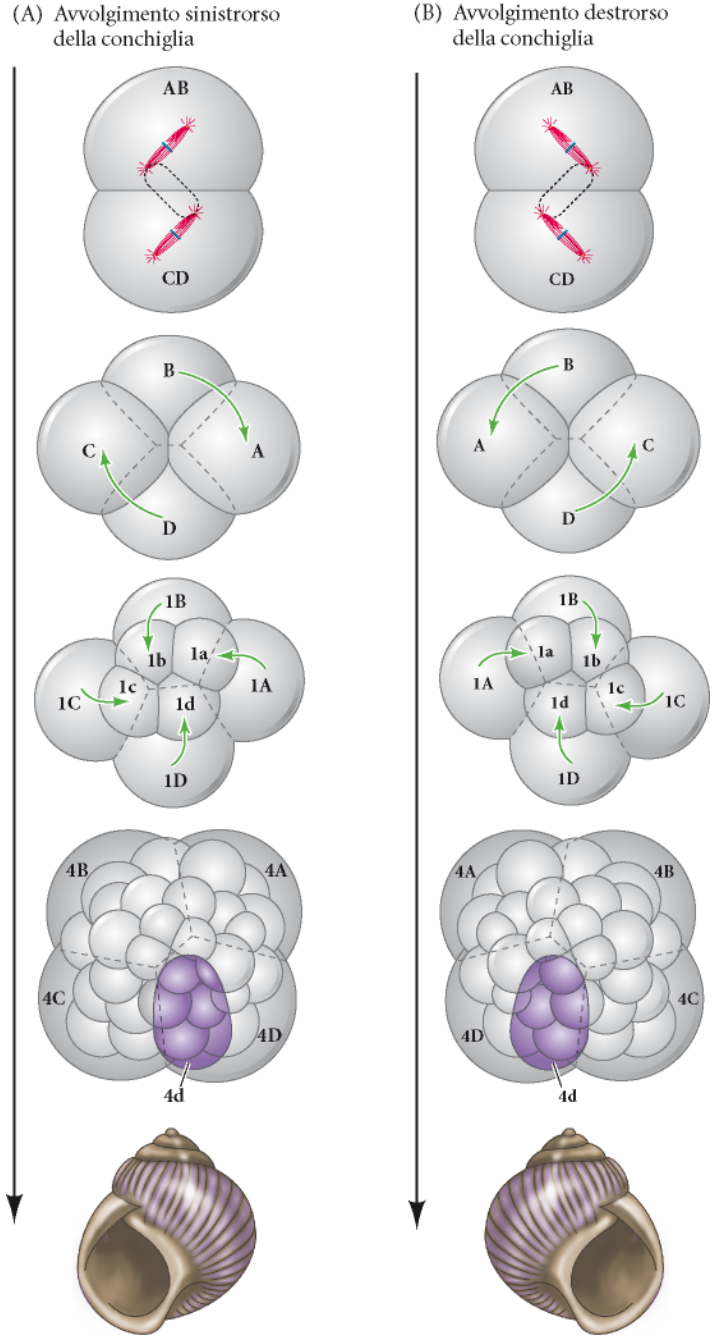

1B
1b
1a
1A
1C
1c
PB
1d
1D

(C)


2B
1b
2A
2b
2c
1a
2C
1c
2a
2d
1d
2D

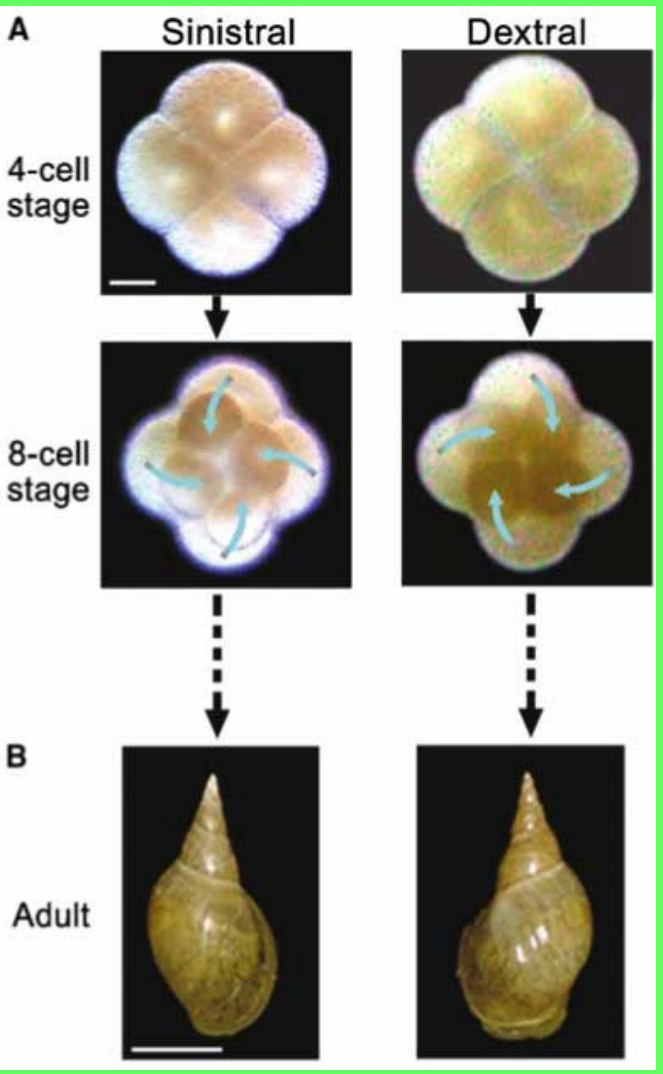
(D)


3b
1b²
2c²
2c¹
3C
3B
2b¹
2b²
3a
3c
1c²
1a²
2d²
2d¹
3A
2a¹
2a²
1d²
3d
3D


(A) Avvolgimento sinistrorso della conchiglia
(B) Avvolgimento destrorso della conchiglia
AB
CD
B
C
A
D
1B
1a
1b
1c
1d
1A
1C
1D
4A
4B
4C
4D
4d

Segmentazione spirale

I piani segmentazione sono diretti obliquamente all´asse animale-vegetativo : I blastomeri sono disposti in modo obliquo. Mancanza di blatocele ⟶ **Stereoblastula**



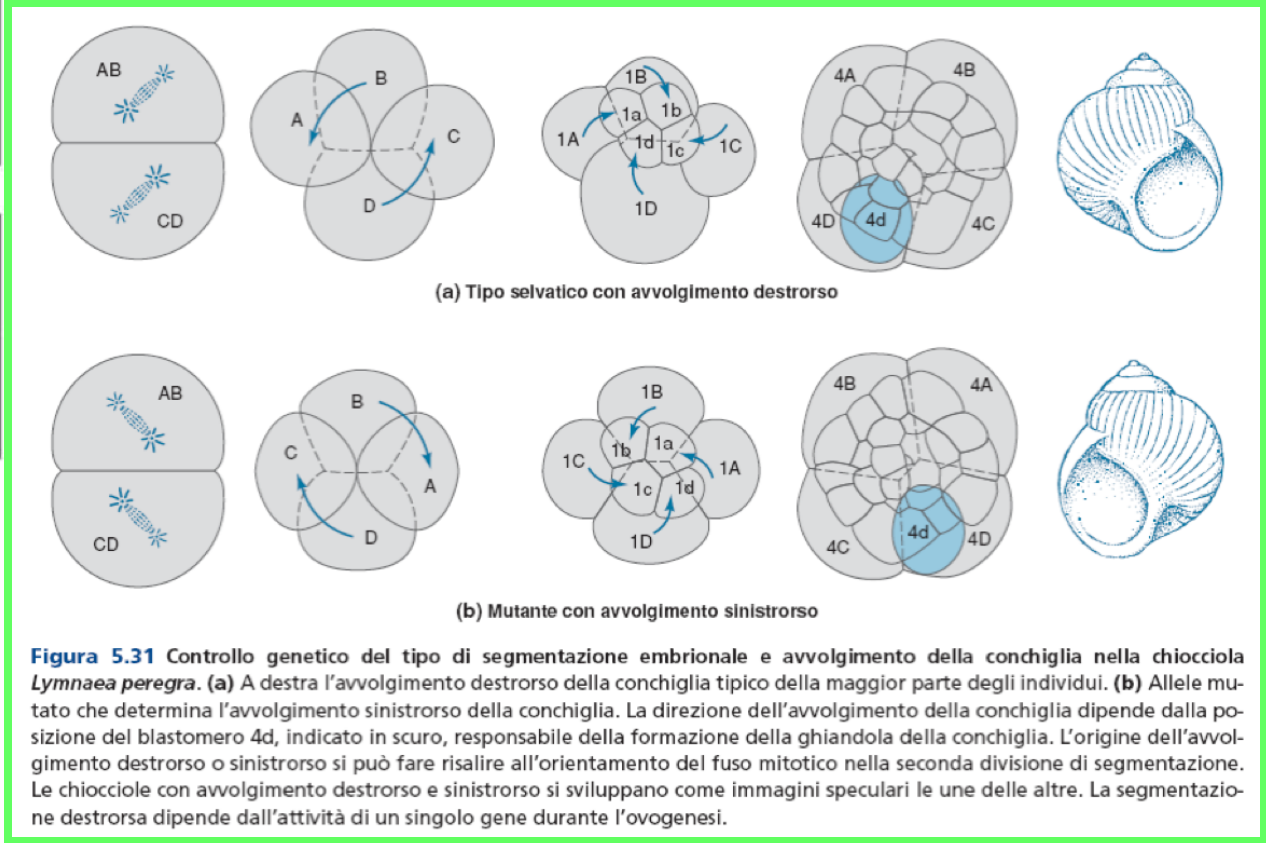
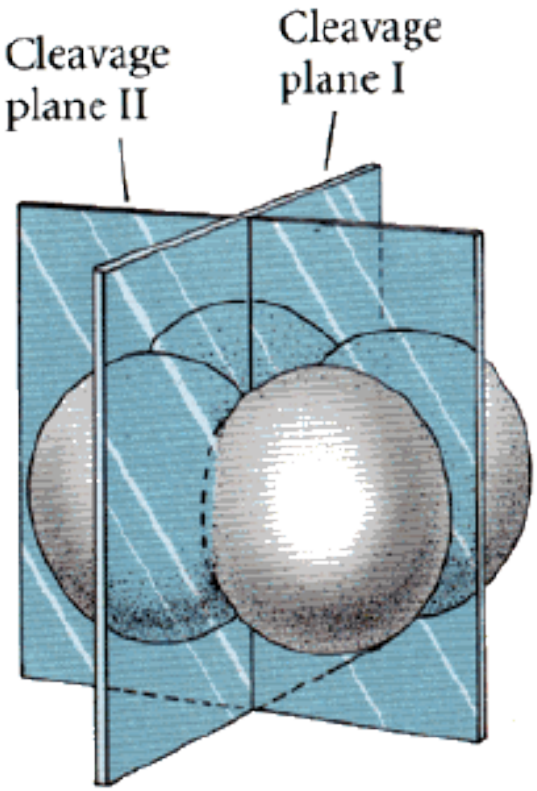


Figura 5.31 Controllo genetico del tipo di segmentazione embrionale e avvolgimento della conchiglia nella chiocciola *Lymnaea peregra*. **(a)** A destra l'avvolgimento destrorso della conchiglia tipico della maggior parte degli individui. **(b)** Allele mutato che determina l'avvolgimento sinistrorso della conchiglia. La direzione dell'avvolgimento della conchiglia dipende dalla posizione del blastomero 4d, indicato in scuro, responsabile della formazione della ghiandola della conchiglia. L'origine dell'avvolgimento destrorso o sinistrorso si può fare risalire all'orientamento del fuso mitotico nella seconda divisione di segmentazione. Le chiocciole con avvolgimento destrorso e sinistrorso si sviluppano come immagini speculari le une delle altre. La segmentazione destrorsa dipende dall'attività di un singolo gene durante l'ovogenesi.

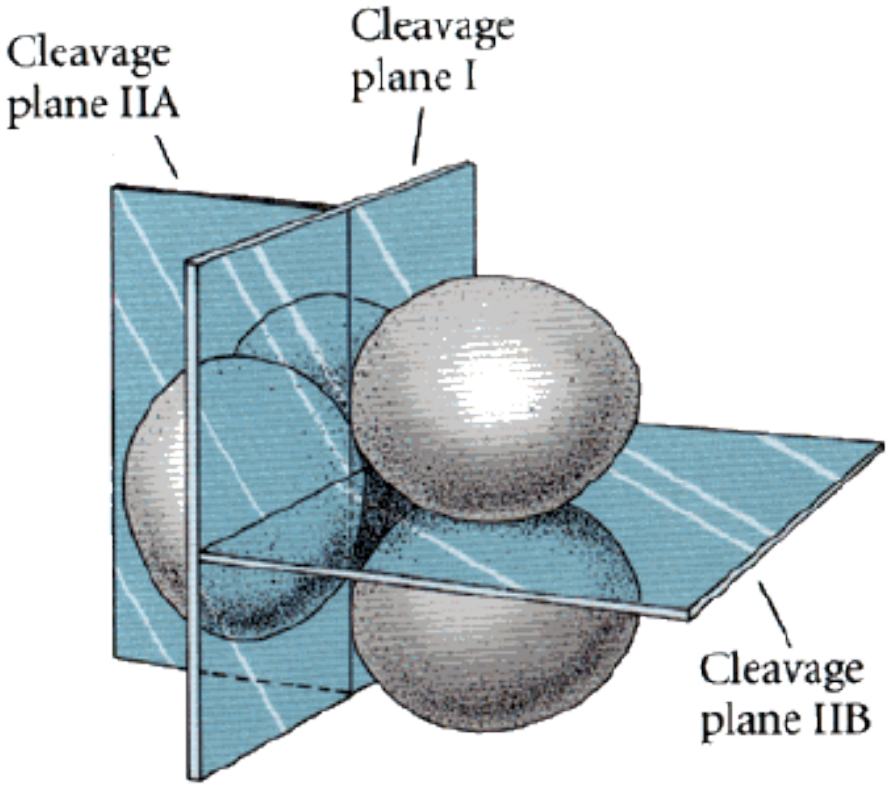
Durante la 4 segmentazione la l´orientamento del fuso si sposta di 90 gradi.

Dai primi 4 micromeri derivane le strutture del capo , dal secondo quartetto la stocisti, organo dell´equilibrio , nei gasteropi la conchiglia

Segmentazione totale rotazionale (Mammiferi)
Piani di taglio iniziali

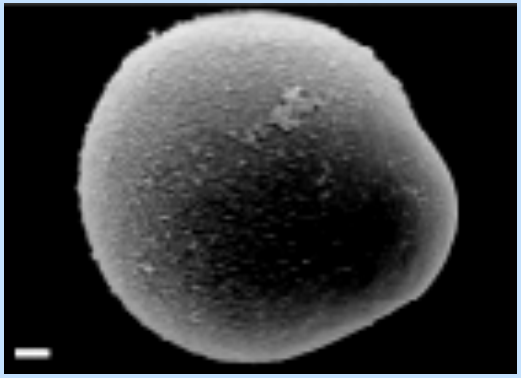


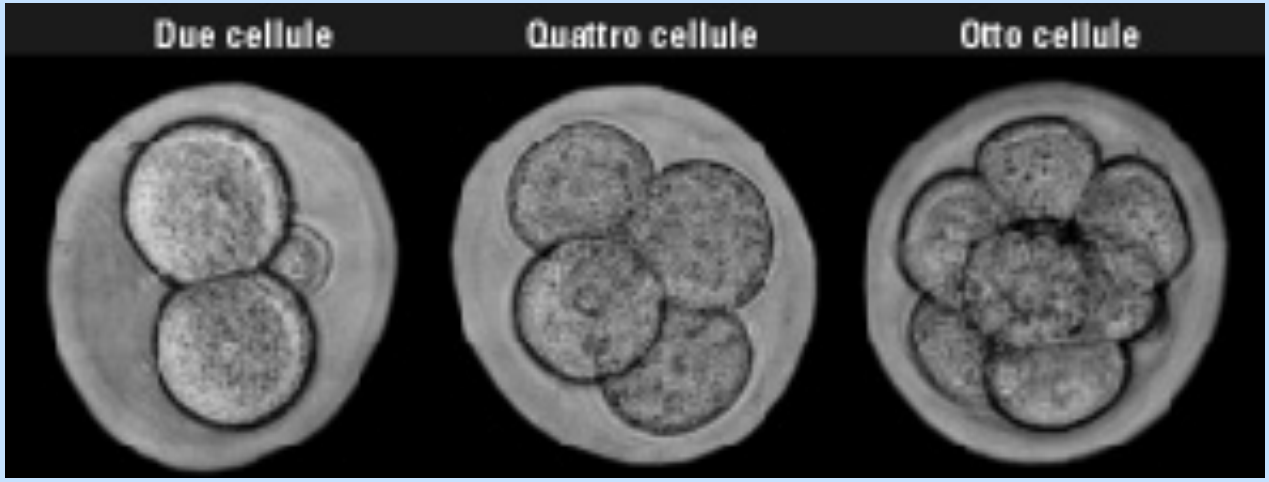
(A) ECHINODERM AND AMPHIBIAN

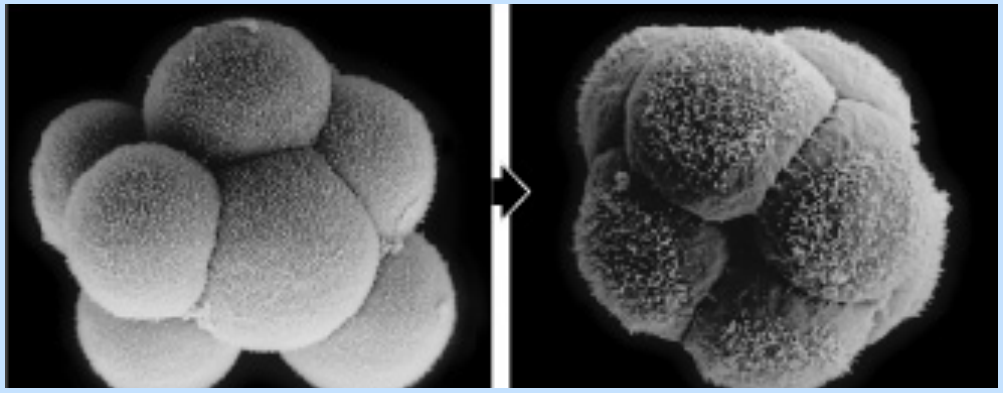


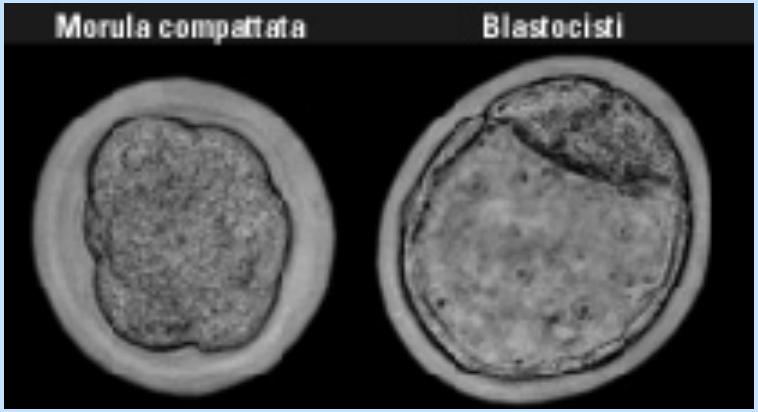
(B) MAMMAL

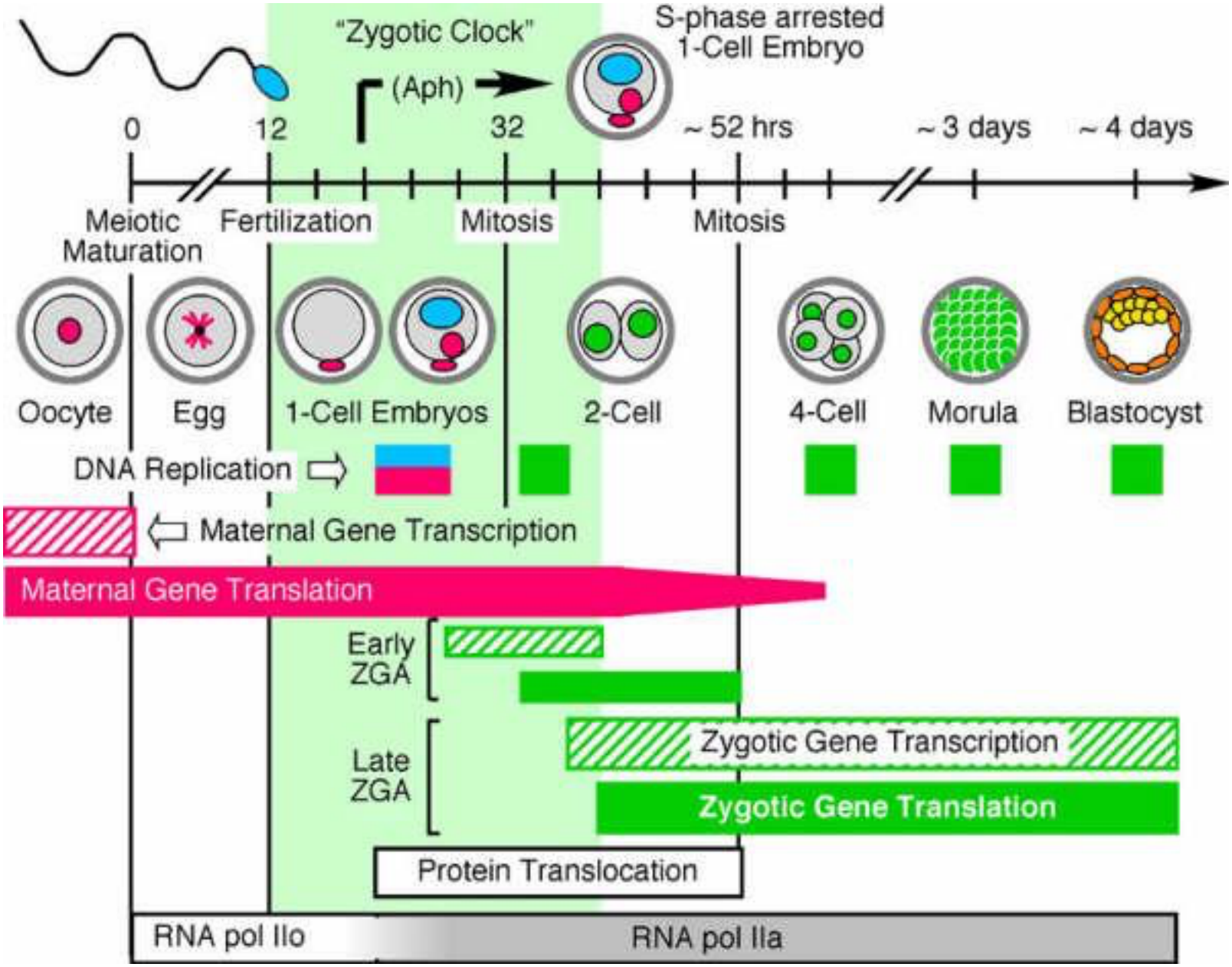
Segmentazione totale rotazionale (mammiferi)

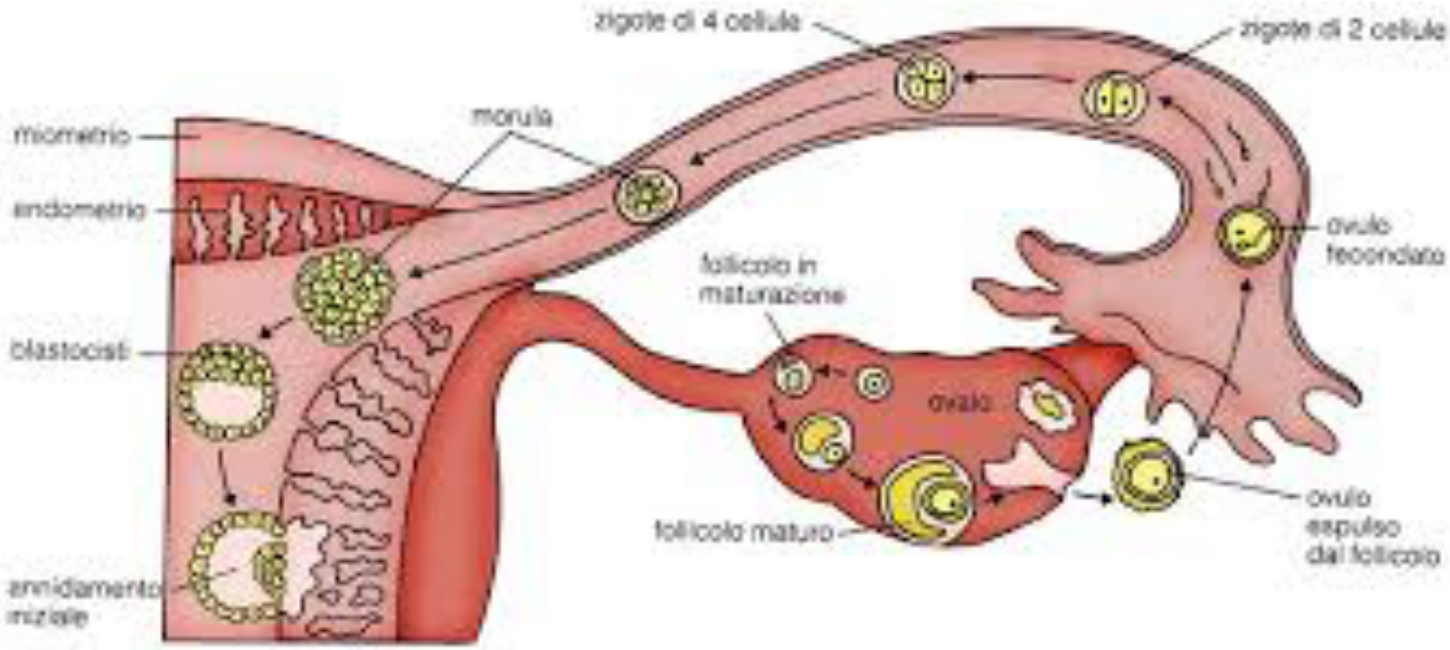




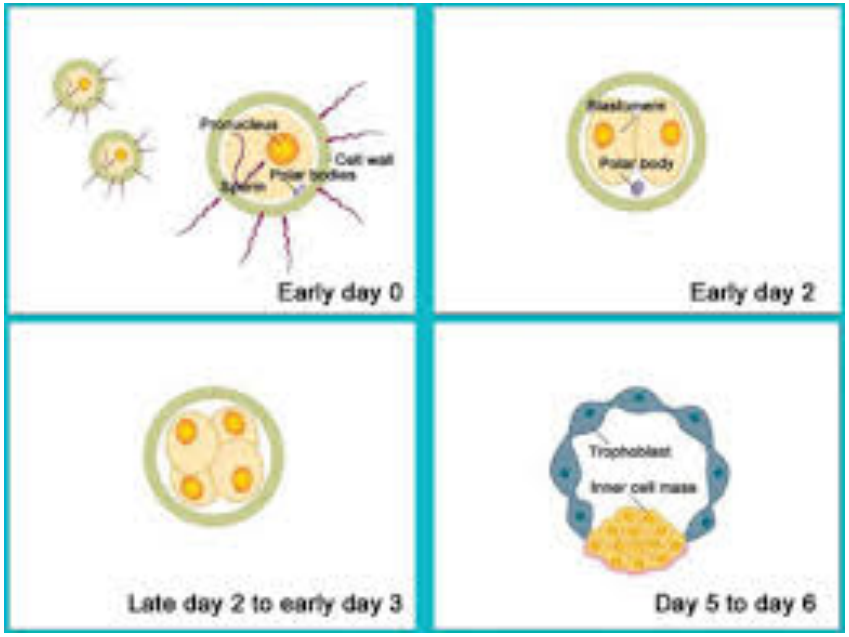


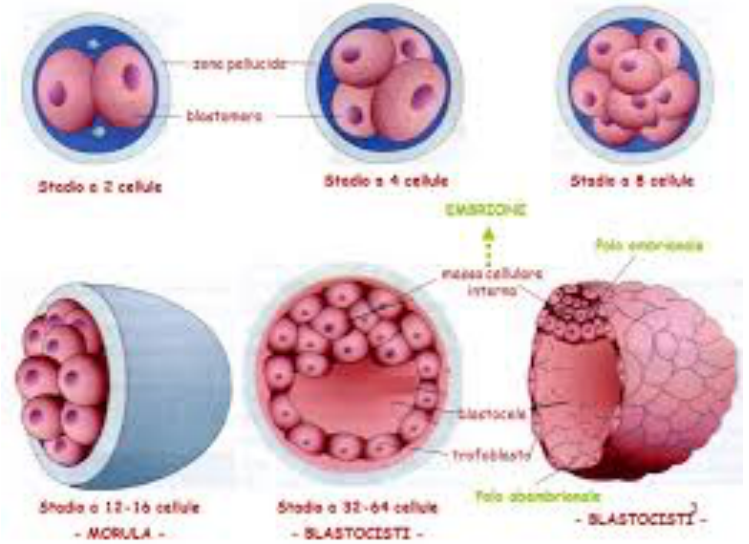


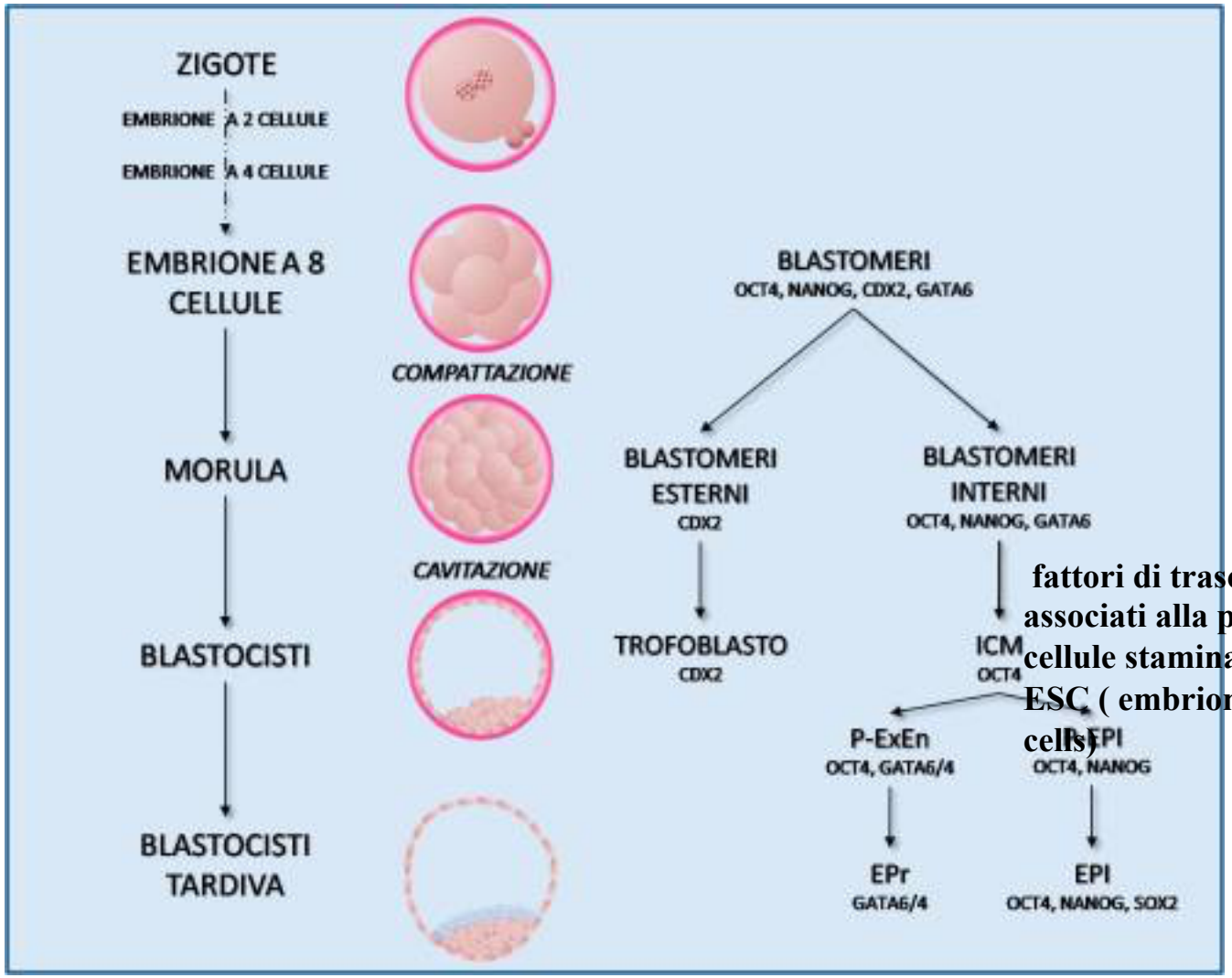

"Zygotic Clock"
(Aph)
S-phase arrested
1-Cell Embryo
0
12
32
~ 52 hrs
~ 3 days
~ 4 days
Meiotic Maturation
Fertilization
Mitosis
Mitosis
Oocyte
Egg
1-Cell Embryos
2-Cell
4-Cell
Morula
Blastocyst
DNA Replication
Maternal Gene Transcription
Maternal Gene Translation
Early ZGA
Late ZGA
Zygotic Gene Transcription
Zygotic Gene Translation
Protein Translocation
RNA pol IIo
RNA pol IIa



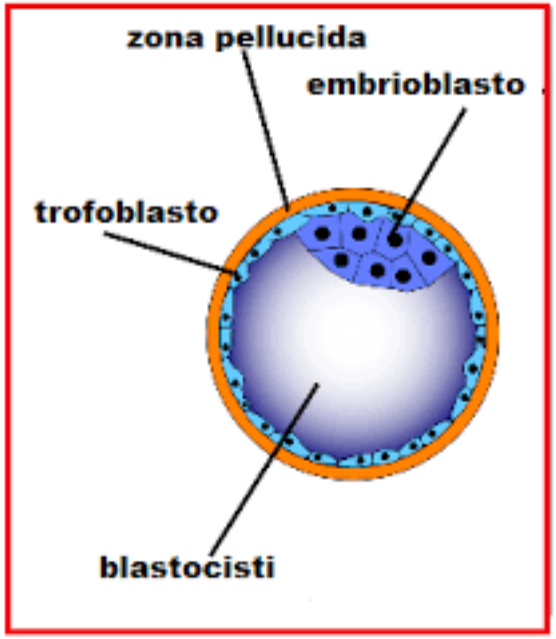
I blastomeri esterni tramite endocitosi attraverso le superfici esterne, iniziano a prelevare fluido dalla cavita´uterina e riversarla in cavità che si sono formate tra i blastomeri, queste si fondono e formano la cavita della blastocisti. Blastocisti 32-64 blastomeri.


Pronucleus
Cell wall
Polar bodies
Sperm
Early day 0
Blastomere
Polar body
Early day 2
Late day 2 to early day 3
Trophoblast
Inner cell mass
Day 5 to day 6


zona pellucida
blastomero
Stadio a 2 cellule
Stadio a 4 cellule
Stadio a 8 cellule
EMBRIONE
massa cellulare interna
Polo embrionale
blastocele
trofoblasto
Polo abembrionale
Stadio a 12-16 cellule
- MORULA -
Stadio a 32-64 cellule
- BLASTOCISTI -
- BLASTOCISTI -

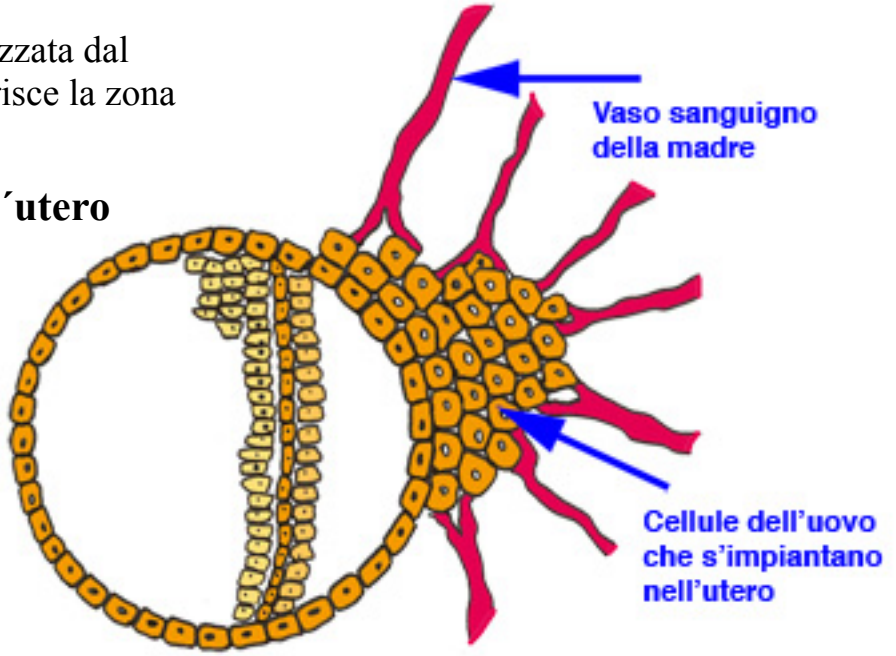


fattori di trascrizione associati alla pluripotenza, cellule staminali embrionali ESC (embrionic staminal cells)

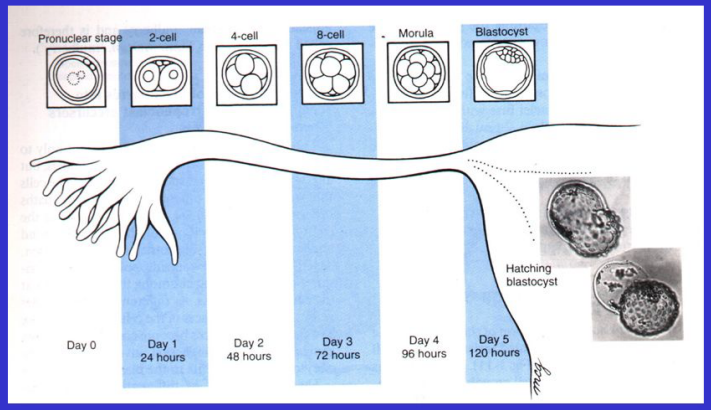


Stripsina: sintetizzata dal trofoblasto digerisce la zona pellucida

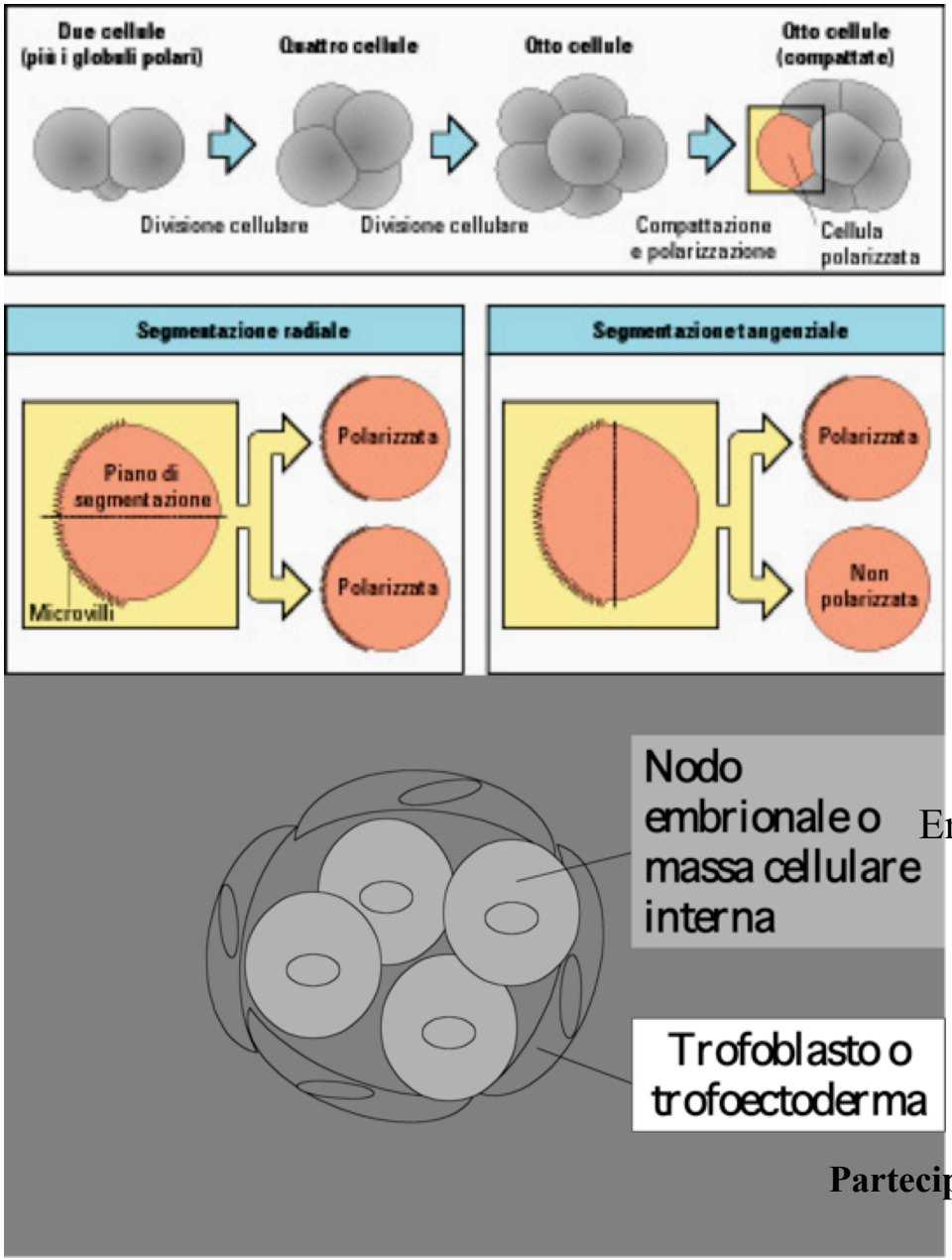
Impianto nell´utero



PRIMA SETTIMANA

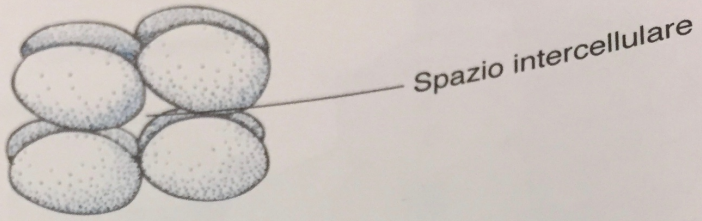


Schema segmentazione mammiferi

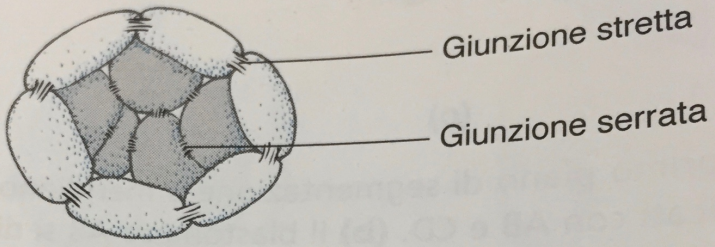


Embrione ed annessi embriona

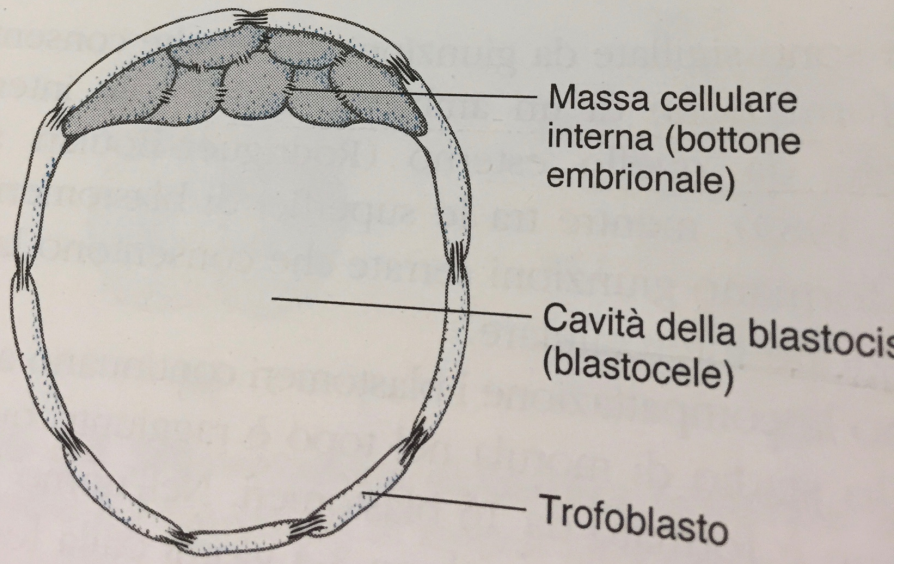
Partecipano alla formazione della plac



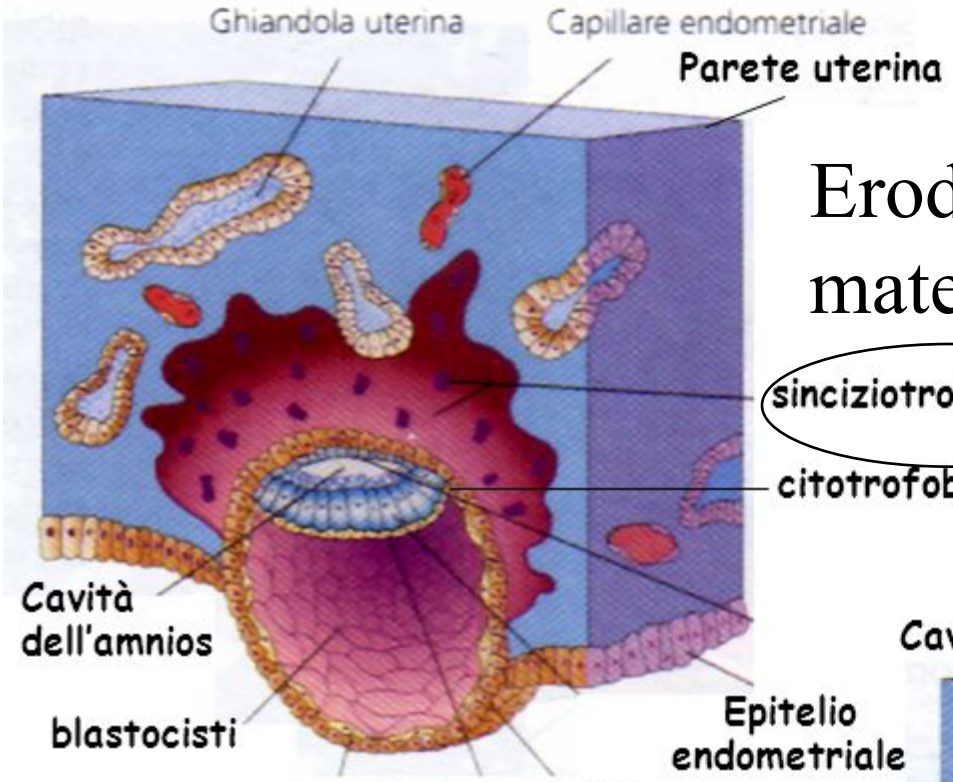
(a) Stadio a 8 blastomeri



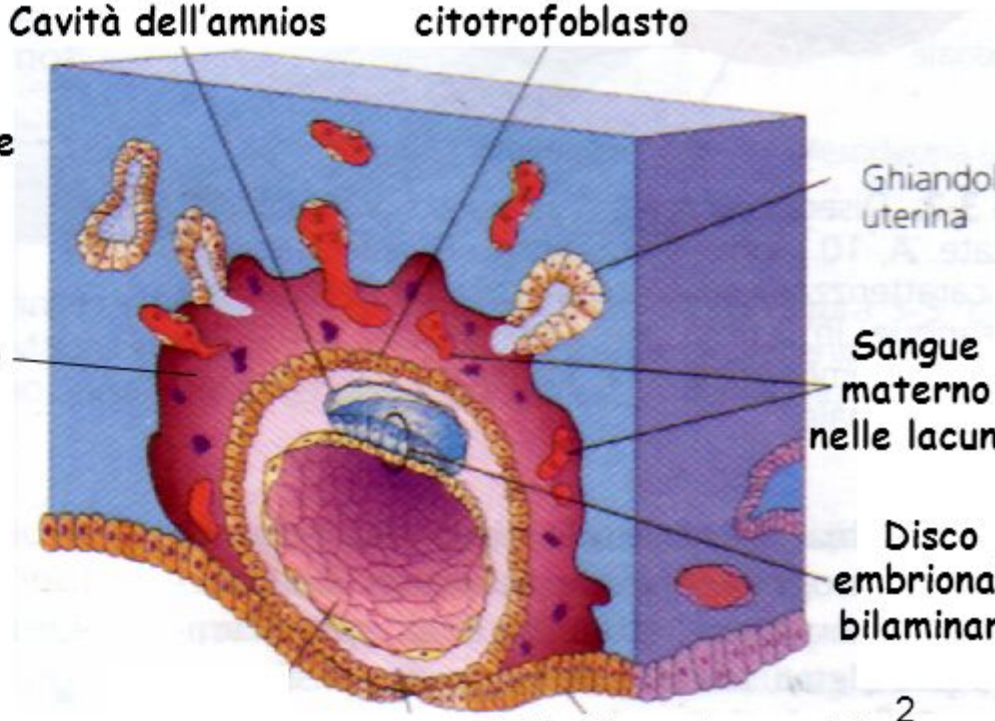
(b) Stadio a 16 blastomeri



(c) Stadio a 32-64 blastom



Erode piccoli vasi sanguigni materni per il nutrimento



6°-9° gg

https://www.youtube.com/watch?v=UgT5rUQ9EmQ

https://www.youtube.com/watch?v=PedajVADLGw