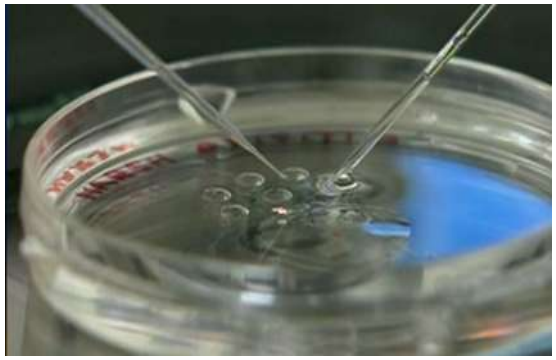
Embryology 2

Fertilization

Capacitation



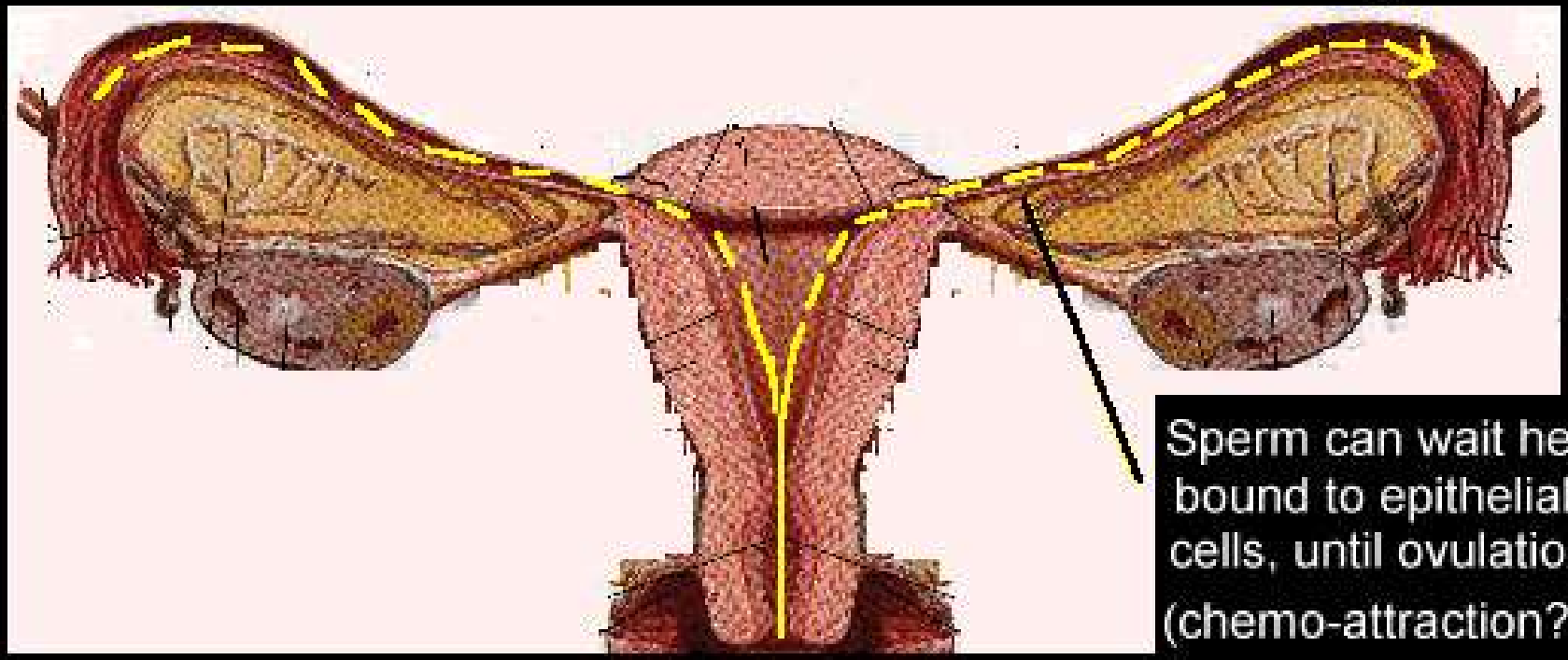
Sperm from ejaculate → Secondary oocyte → (nothing)

Sperm from uterus → Secondary oocyte → Fertilization

Capacitation

- Glycoprotein and sterol coat acquired in epididymis is removed by proteases in the uterine/ cervical fluid.
- This causes the cell membrane to become more permeable to calcium ions
- These (indirectly, via cAMP) activate strong tail lashing and make the acrosome reaction possible later.

Fertilization takes place here



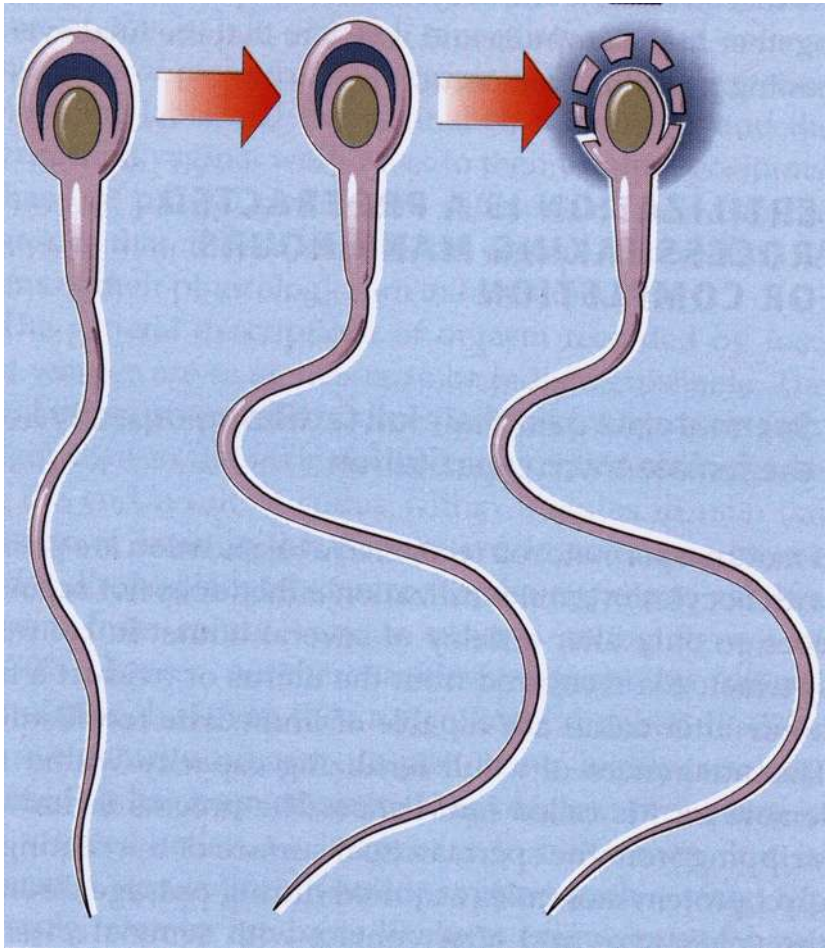
Sperm can wait here, bound to epithelial cells, until ovulation.

(chemo-attraction??)

When sperm meet the Zona Pellucida of the egg, they undergo an Acrosome Reaction;

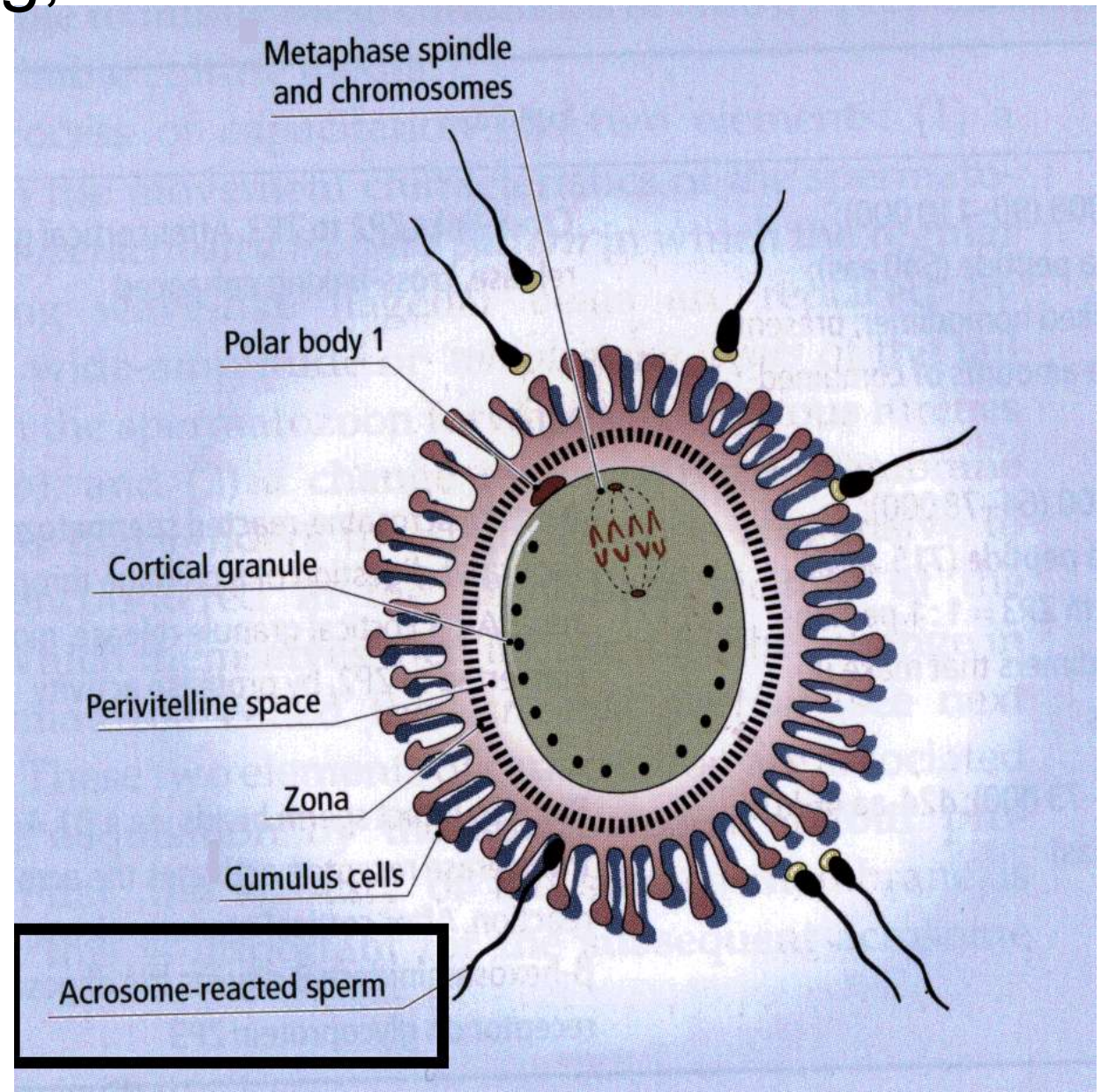
Acrosome membrane and plasma membrane fuse at many points

Acrosomal contents spill out and can digest the zona pellucida



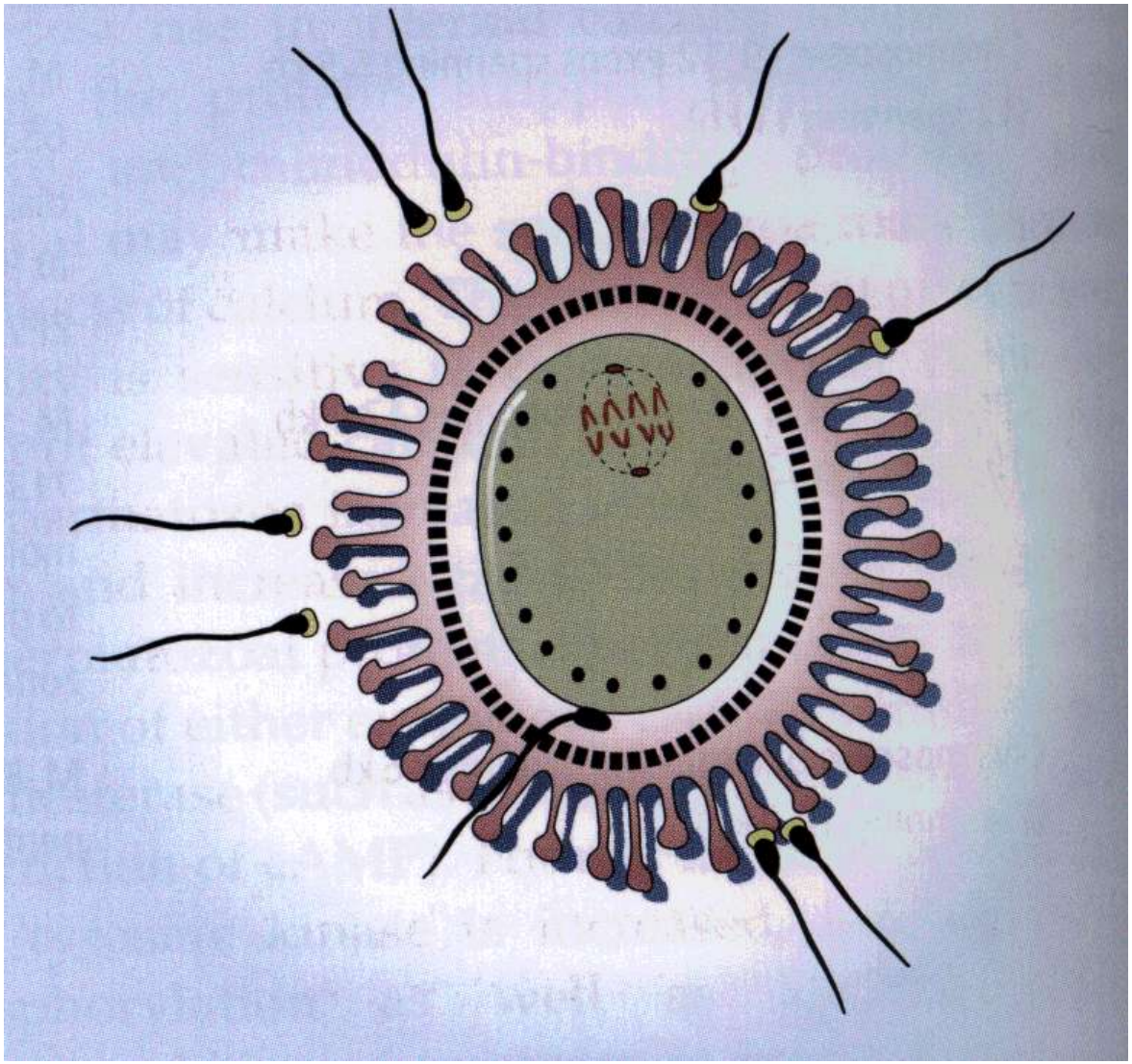
Pic: Johnson Essential Reproduction.

Acrosome reacted sperm burrow towards egg;



Pic: Johnson Essential Reproduction.

One sperm reaches the egg membrane;

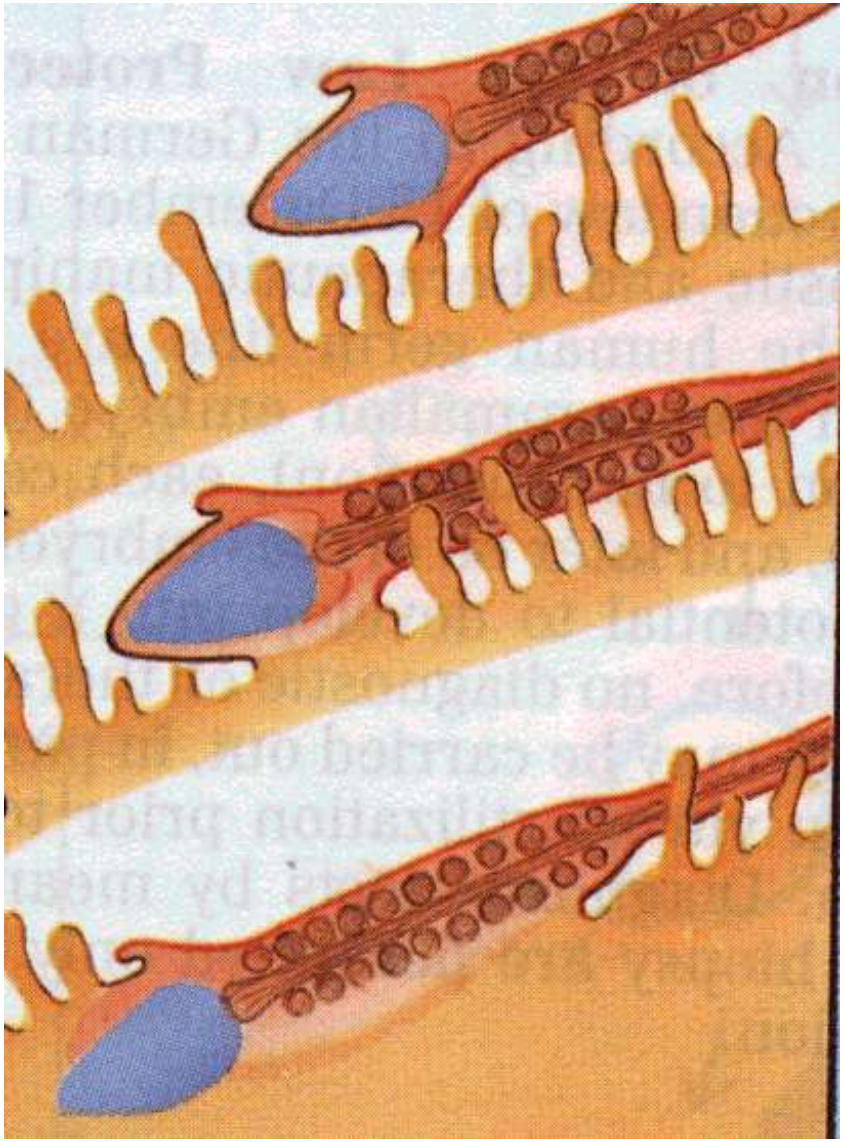


Pic: Johnson Essential Reproduction.

And fuses with the membrane;

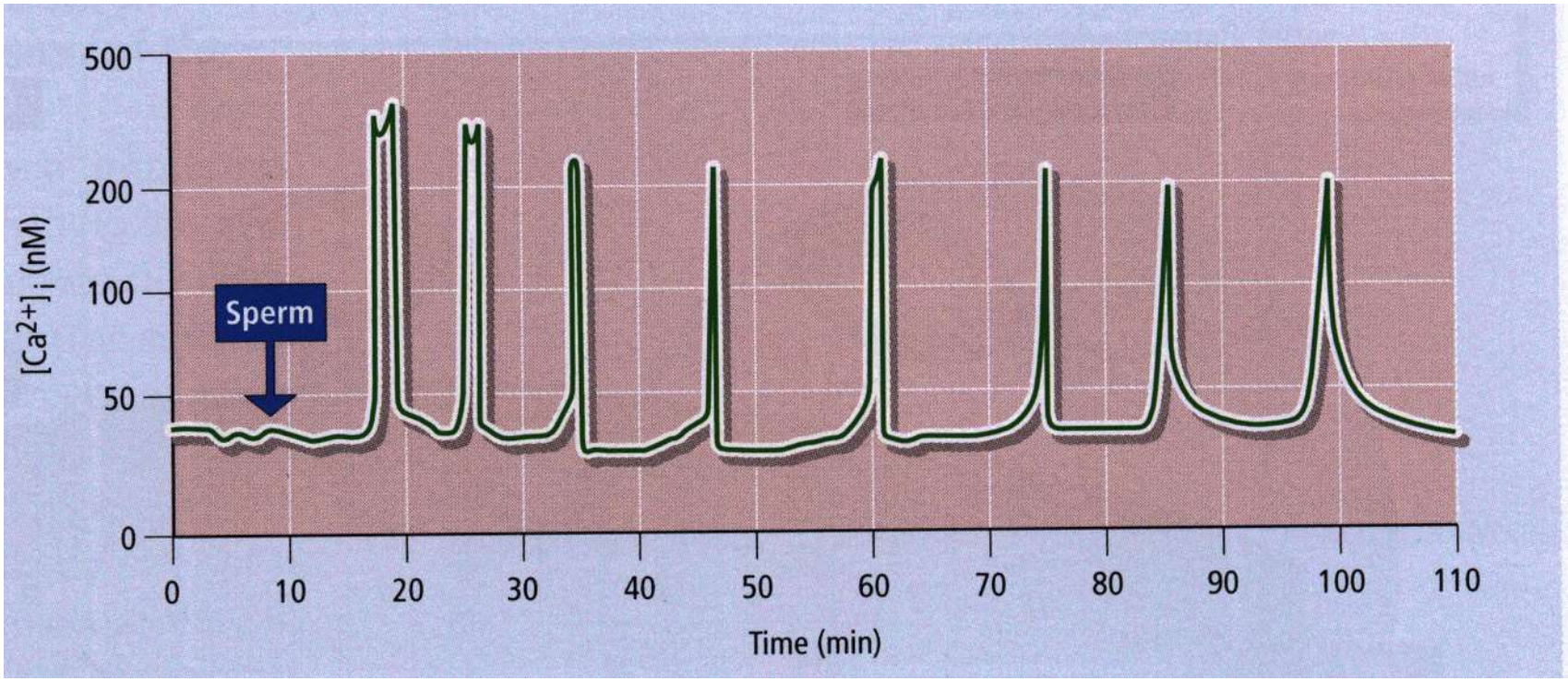
Only sperm that have undergone the acrosome reaction can do this

Fusion causes a wave of calcium entry, which keeps repeating



Pic: Johnson Essential Reproduction.

Calcium waves in the oocyte following sperm entry

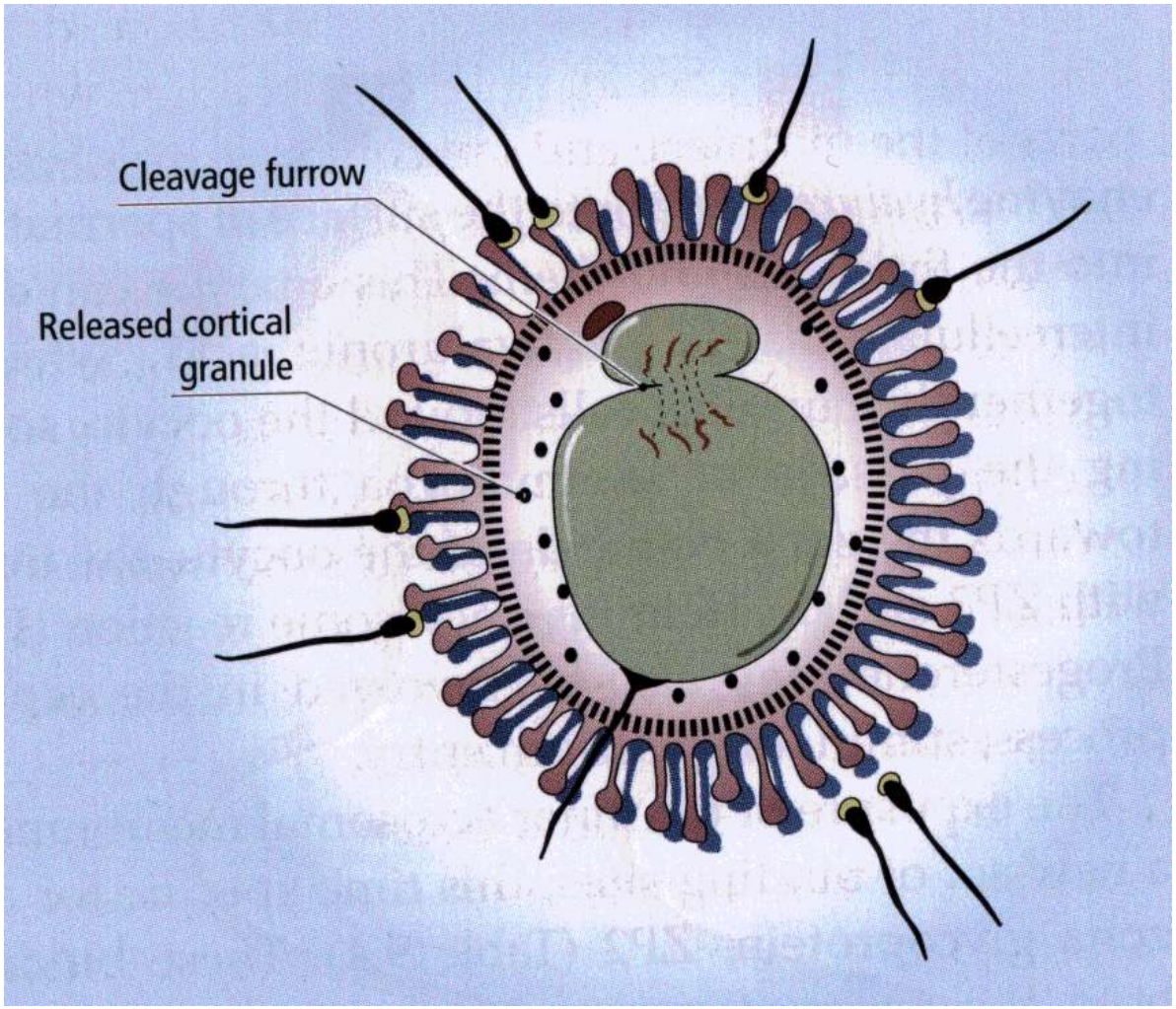


Pic: Johnson Essential Reproduction.

Calcium waves have two effects;

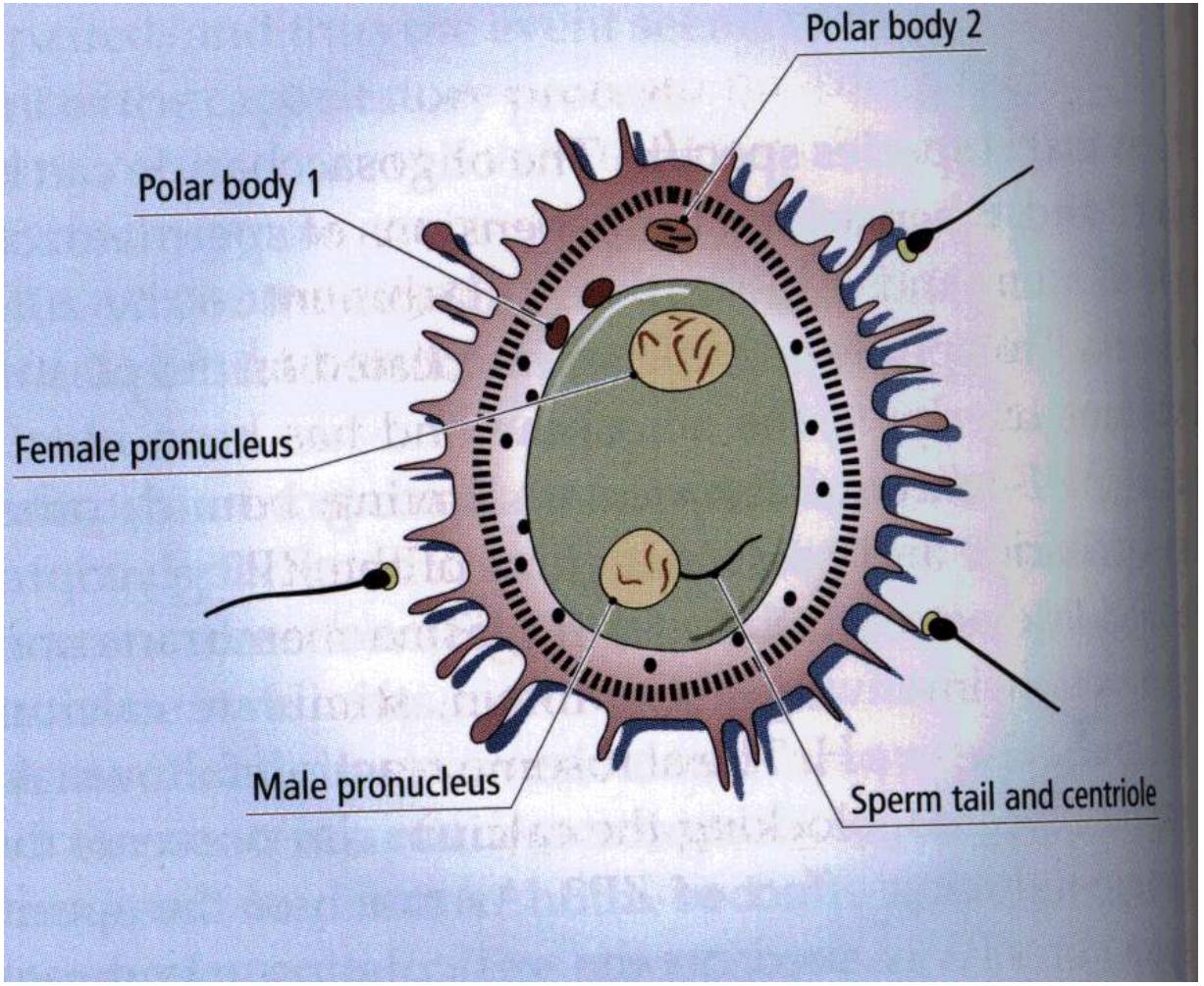
1 – cortical granules are released; these alter the ZP and make it impenetrable by sperm (and also block fusion)

2 - Meiosis of the oocyte resumes



Pic: Johnson Essential Reproduction.

Chromosomes decondense and form the male and female pronuclei;



Pic: Johnson Essential Reproduction.

Assisted fertilization

Assisted fertilization

Typical reasons

Blocked/ absent oviducts (pelvic inflammatory disease – *Chlamydia* or *Gonorrhoea* often damage oviducts; also congenital absence, endometriosis of earlier elective tubal ligation).

Blocked vasa deferentia/ eferentia; impotence; low male fertility

Female age

Edwards (holding Louise Brown, the first IVF baby) and Steptoe, 1978

Assisted fertilization

Typical stages:

Superovulation (discussed in lecture 1)

Oocyte harvesting (follicular aspiration: laparoscopic or TV), from would-be pregnant woman or from a donor.

Sperm harvesting (usually masturbation: can be by aspiration from epididymis or even testis for ICSI).

Capacitation of sperm (artificially)

Mixing of sperm and oocytes.

Observation of early development (often genetic testing of 1 cell)

Embryo transfer.

FHS/ LH analogues; blood oestrogen used not monitor results

Image credit: Dr Malpini's blog (a blog about IVF)

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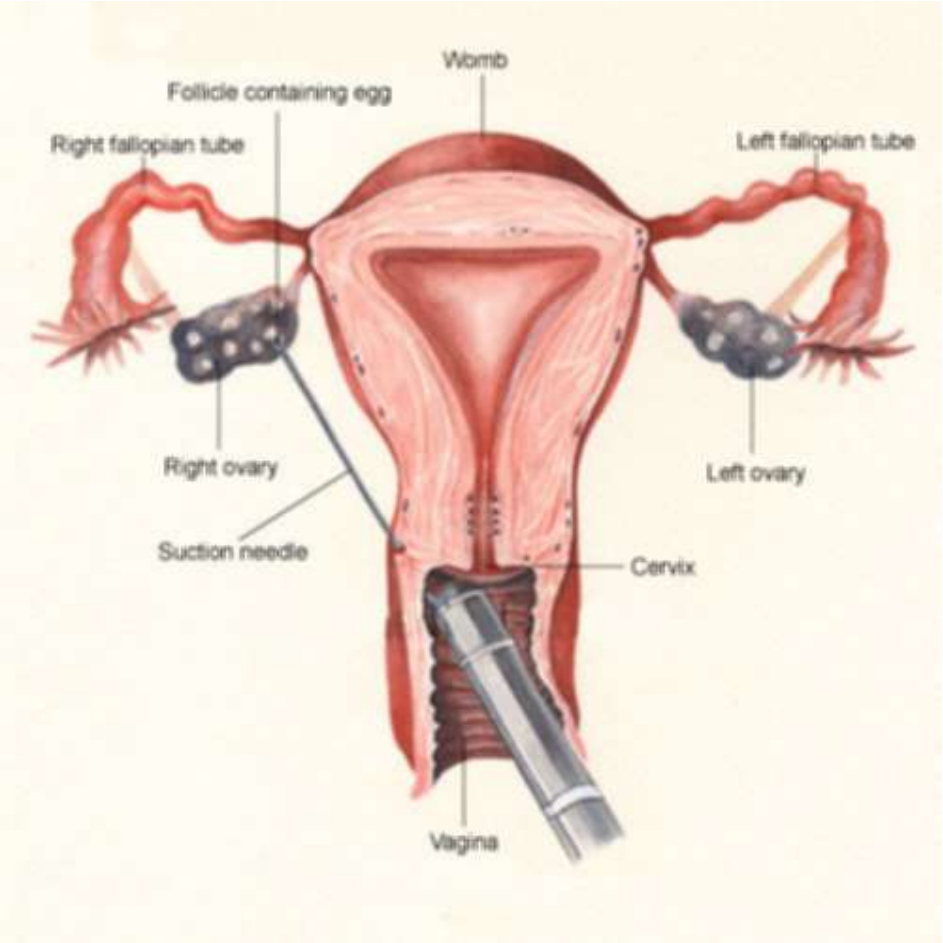
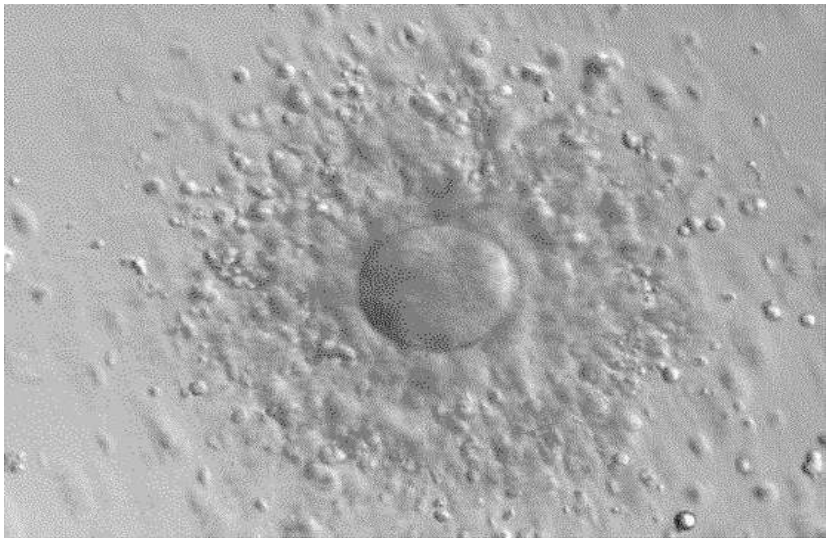
Transvaginal oocyte harvesting (has largely replaced laparoscopy)



with the patient lying on her back, knees up, the geometry works out more easily than this ‘upright’ diagram implies.

Image credit: medical-artist.com

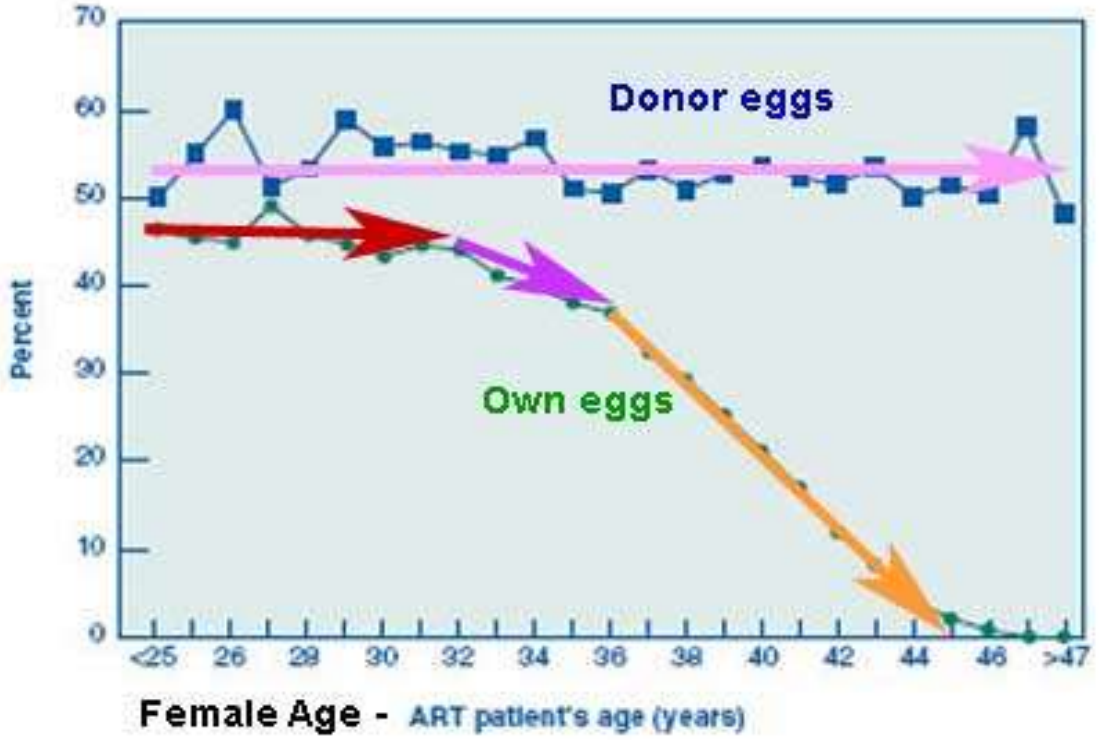
Oocyte straight from follcile, with accompanying granuosa cells



Cleaned up ('naked') oocyte

Image credit: 'Ekem' (Creative Commons)

Percentages of Transfers That Resulted in Live Births for ART Cycles Using Fresh Embryos from Own and Donor Eggs, by ART Patient's Age, 2005



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Capacitation medium (typical):

salts (osmolarity and correct membrane voltages)

human serum albumin (mops up sterols from sperm surface)

lactate, pyruvate, often glucose (energy)

$CaCl_2$ for elevating Ca^{2+} in the cells

bicarbonate (both a pH buffer and an activator of adenylyl cyclase, normally activated by the Ca^{2+} influx).

heparin may be used to make the acrosome reaction more likely (looks like the GAGs in the zona pellucida, to some receptors on sperm)

Do not try to learn this 'recipe': the point to take away is that a lot of care needs to be taken to mimic the female environment

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ICSI

Intra-Cytoplasmic Sperm Injection

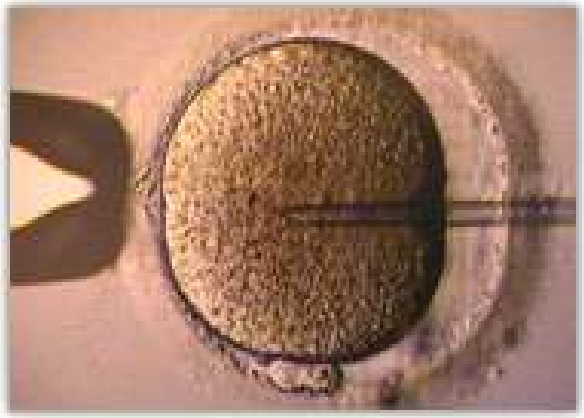

Image credit: J Antonius CC-2.0 via Wikimedia Commons

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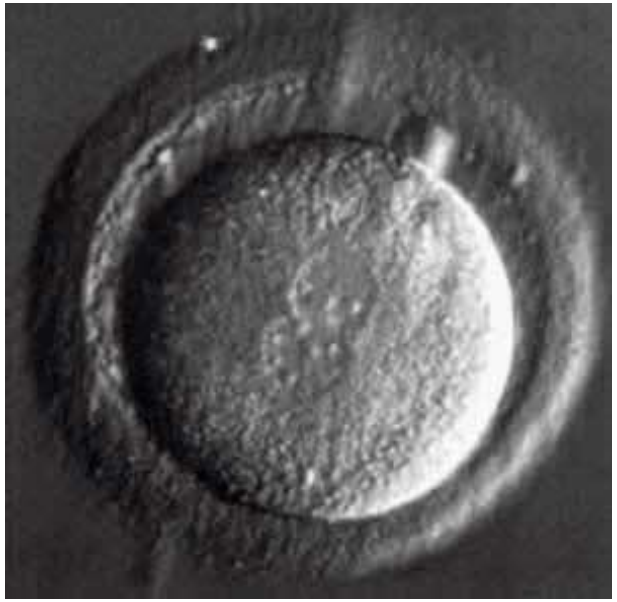
Quality control



Apparently normal diploid

Abnormal triploid (reject!).

Assisted fertilization

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Embryo transfer (PV, guided by ultrasound).

This process shows parents a view of their offspring much younger than other parents see, even with ultrasound;

Image credit: still from Matt and April's Youtube video: https://www.youtube.com/watch?v=CFf9wVsapD8

Normal development – to implantation

The new embryo has to;

Grow much bigger (adult humans are approx 1,000,000 times larger than a fertilized egg: 80 litres vs approx 80 microlitres)

Create internal differences (so what is one cell becomes many cell types)\

Organize the axes and the complex anatomy of the body

THIS IS NOT JUST THE READING OF A 'GENETIC BLUEPRINT'

Engineering blueprints	Genes
The shape of the blueprint depicts the final structure.	The physical shape structure of genes bears no direct relation to the structure of the body.
The blueprint is not part of the structure.	Genes are part of the body
Builders, who are not themselves part of the structure, do the building	There are no external builders
The builders bring in knowledge and information from outside	There are very few opportunities for bringing in inside information
The building/ car/ plane only has to function when it is finished.	The body has to function well enough to live at all stages.

Job 1: making a difference

To have cells of distinct types, one first needs more than one cell.

“Cleavage” (mitosis with no growth);

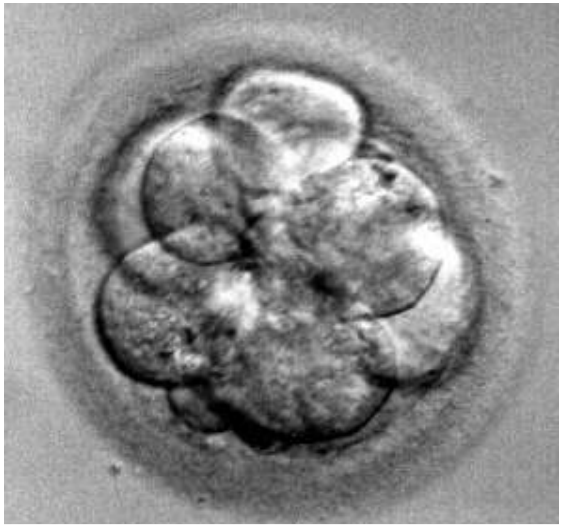


Image credit: Miranda Bernhardt (Creative Commons)

Activation of the embryonic genome

At the 4 cell stage –

mRNA synthesis from embryo's own DNA begins

maternal mRNA is destroyed at an increasing rate.

“Cleavage” (mitosis with no growth);

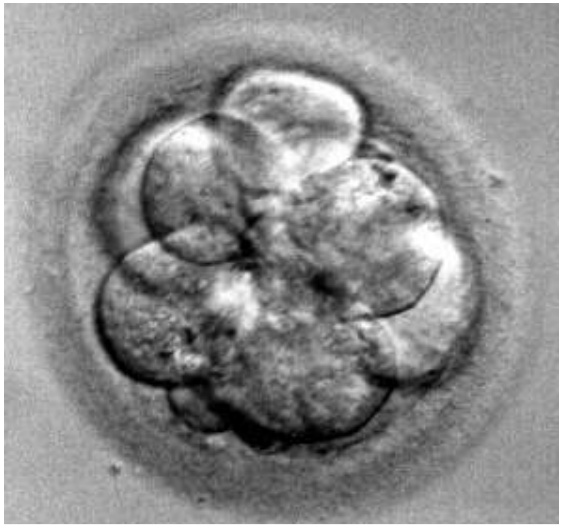


Image credit: Miranda Bernhardt (Creative Commons)

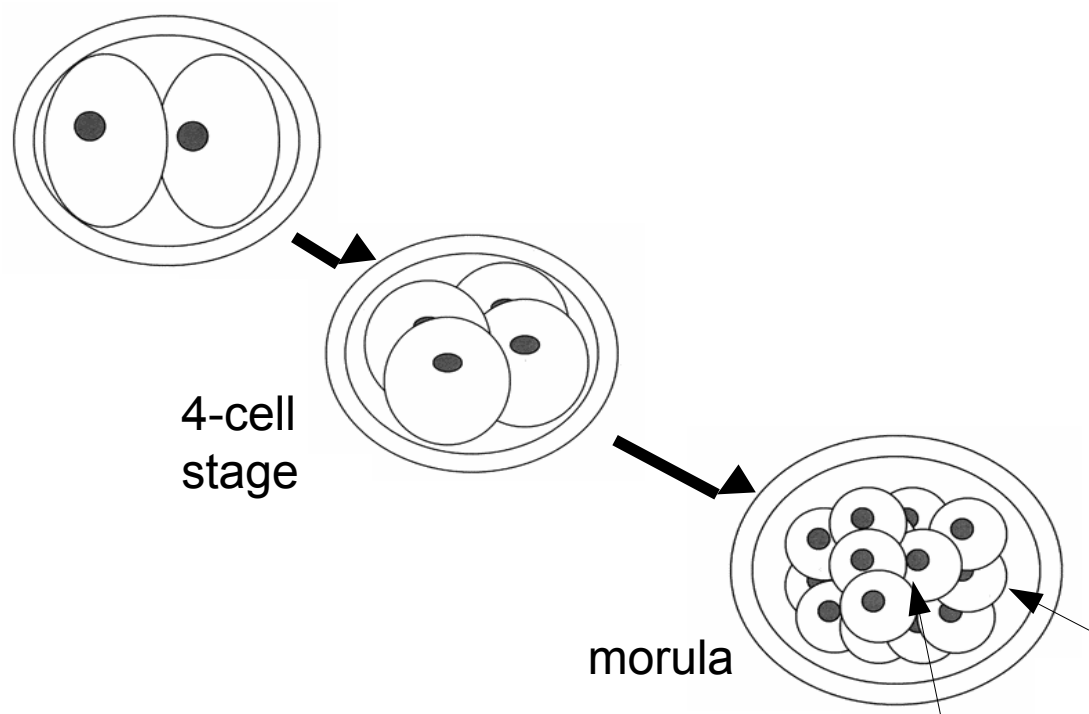
Job 1: making a difference

To have cells of distinct types, one first needs more than one cell.

OK – so now we have lots of cells.

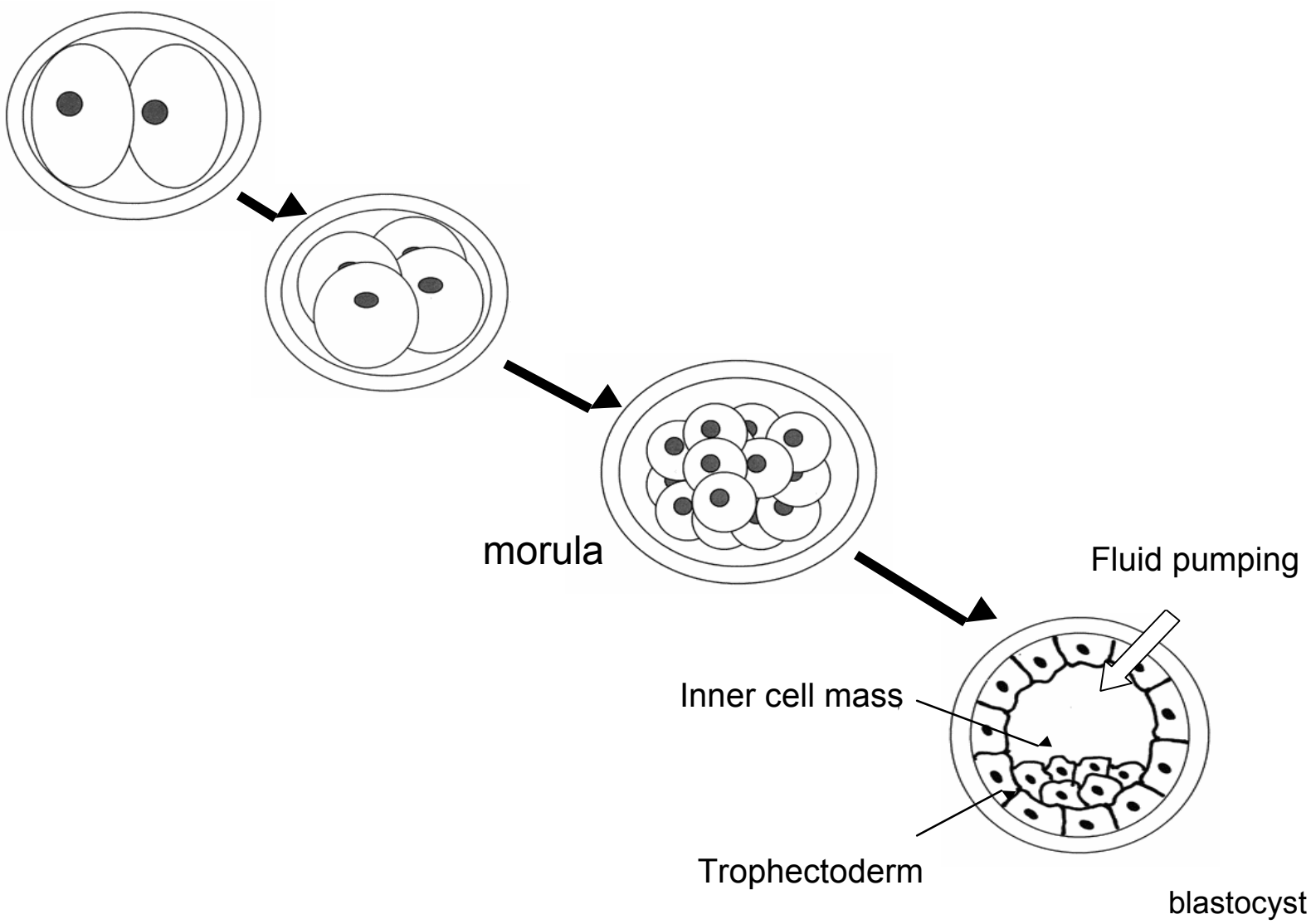
> How can we make them different ???

Bring in extra information using the mathematical rules of geometry



Cells on the inside have contact all round. Cells on the outside have a free surface.

This is the first difference, and the embryo uses it.


morula
Fluid pumping
Inner cell mass
Trophectoderm
blastocyst

The inner cell mass makes the body itself, plus some extra-embryonic membranes

This layer, the trophoblast, will make placenta and some other extra-embryonic material

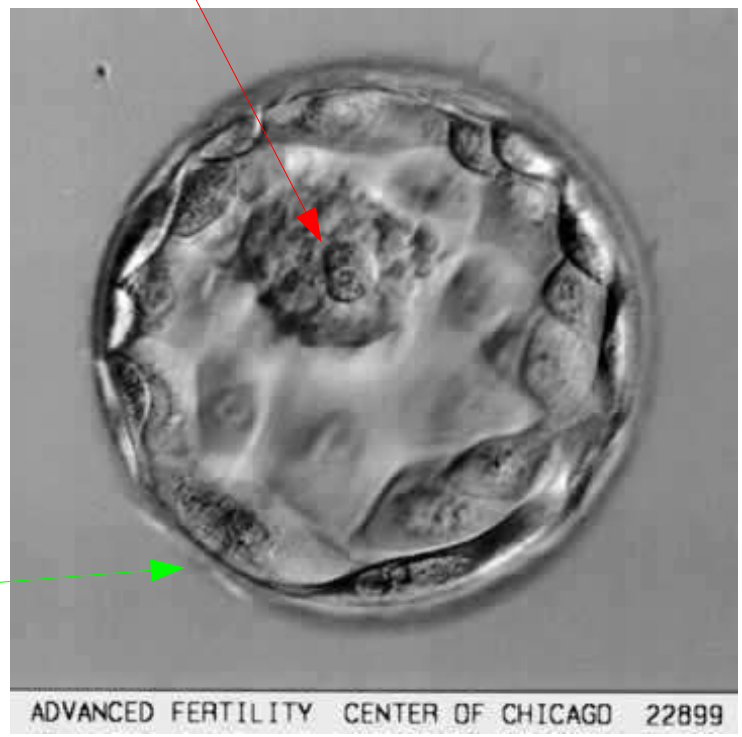
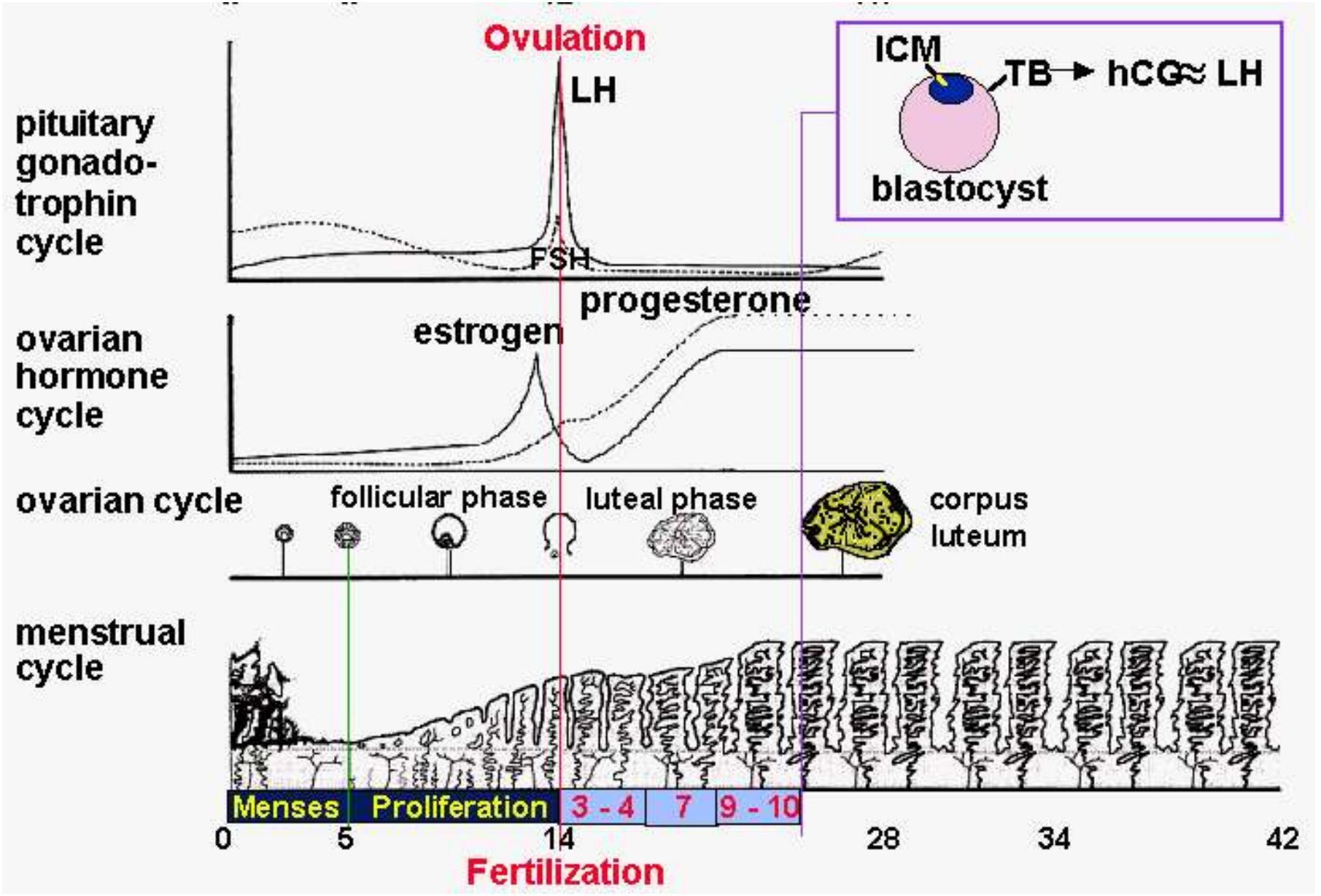
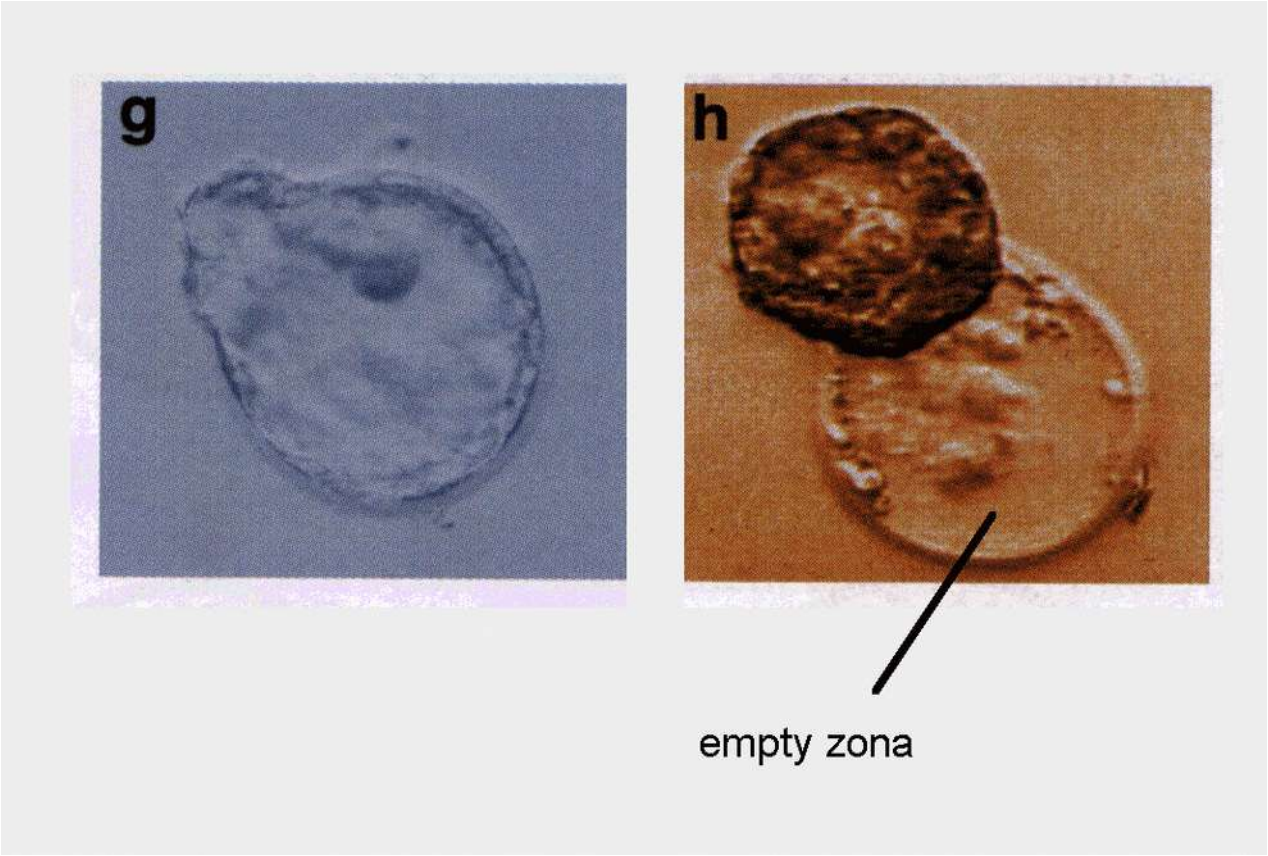


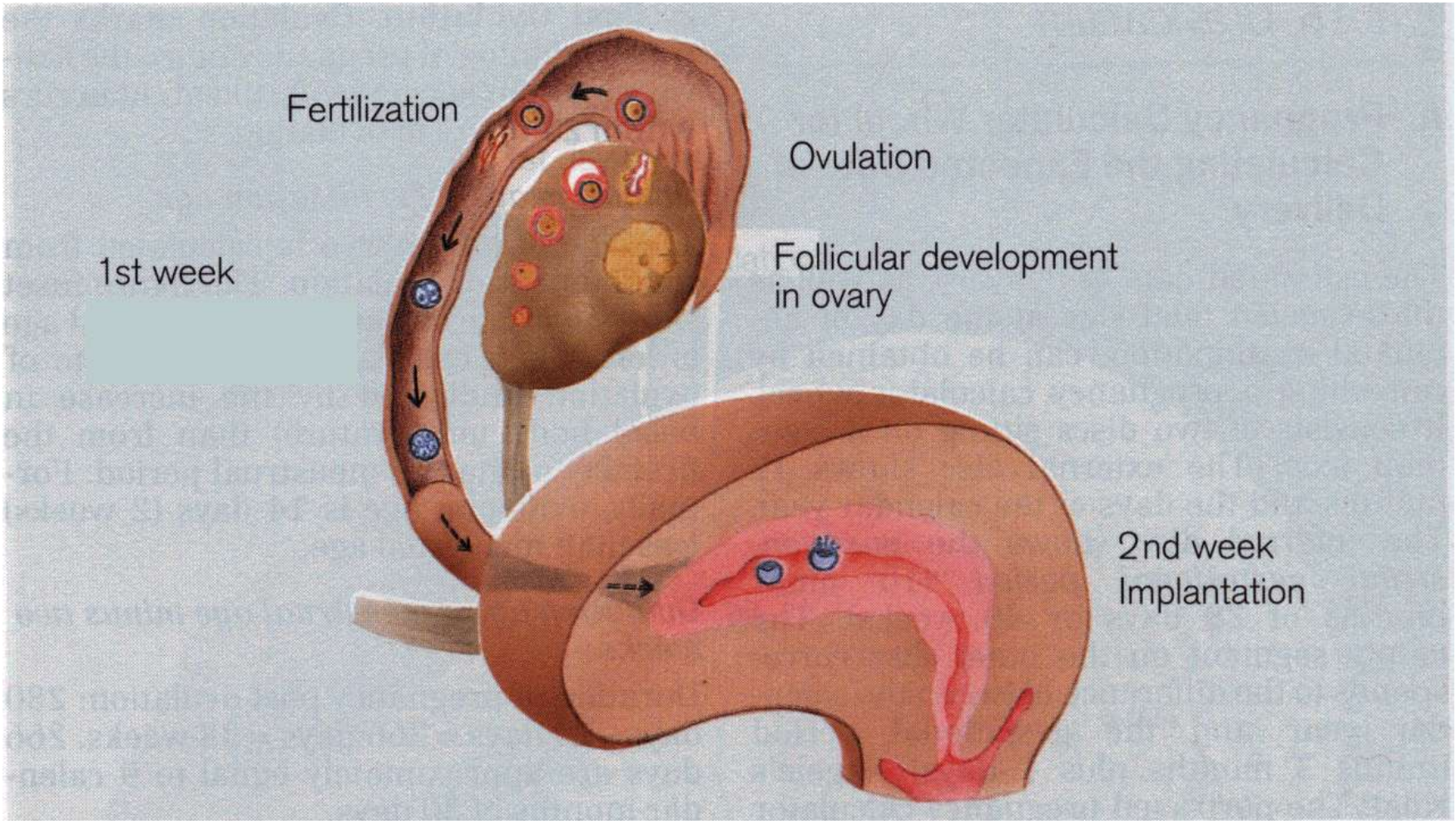
Image Credit: AFC Chicago (Creative Commons)


Ovulation
ICM
TB → hCG≈ LH
blastocyst
pituitary gonado-trophin cycle
LH
FSH
progesterone
ovarian hormone cycle
estrogen
ovarian cycle
follicular phase
luteal phase
corpus luteum
menstrual cycle
Menses
Proliferation
3 - 4
7
9 - 10
0
5
14
28
34
42
Fertilization

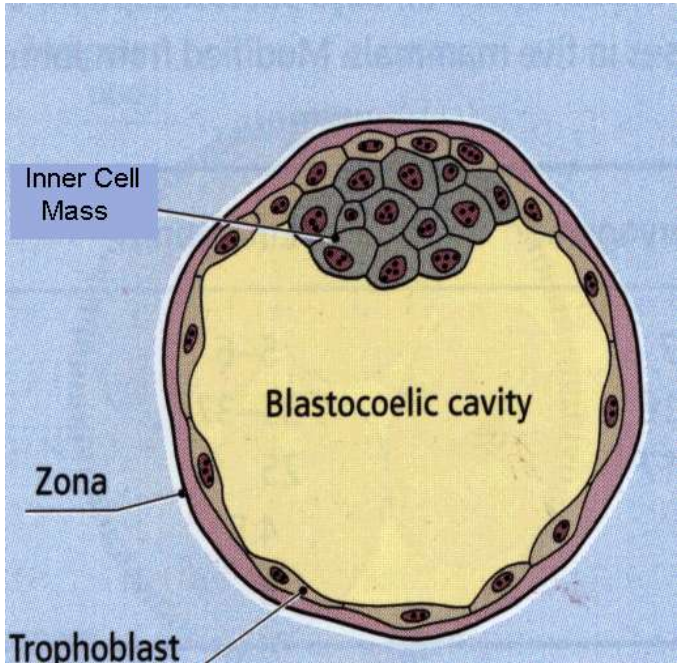
Blastocyst ‘hatches’ through Zona Pellucida;

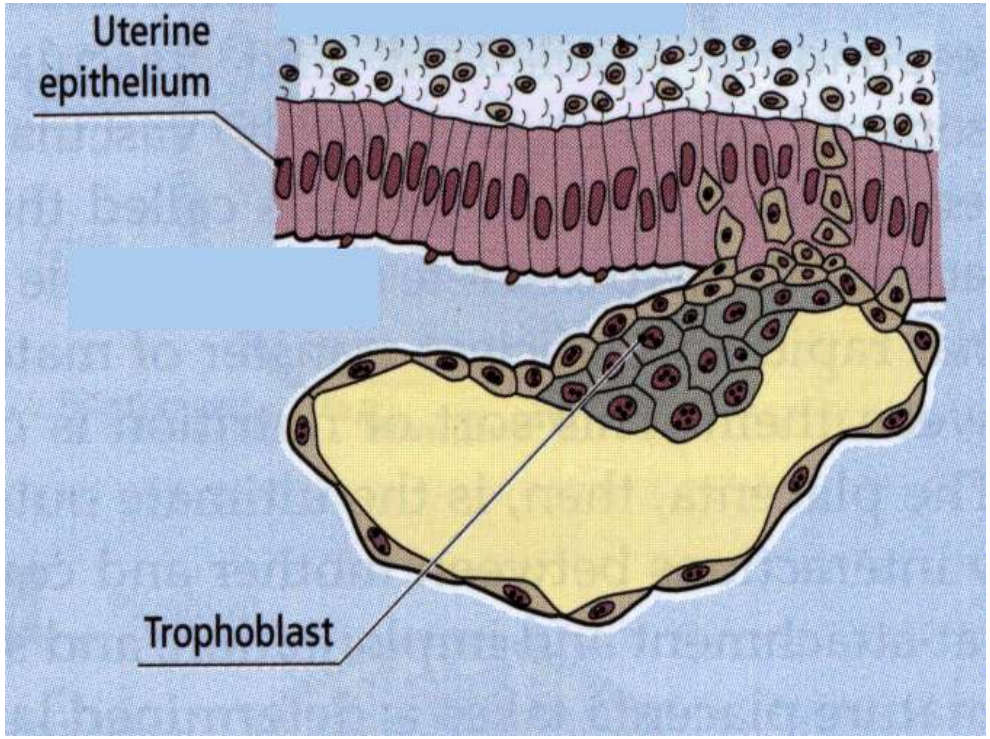


The early embryo lives unattached on its journey down the fallopian tube;



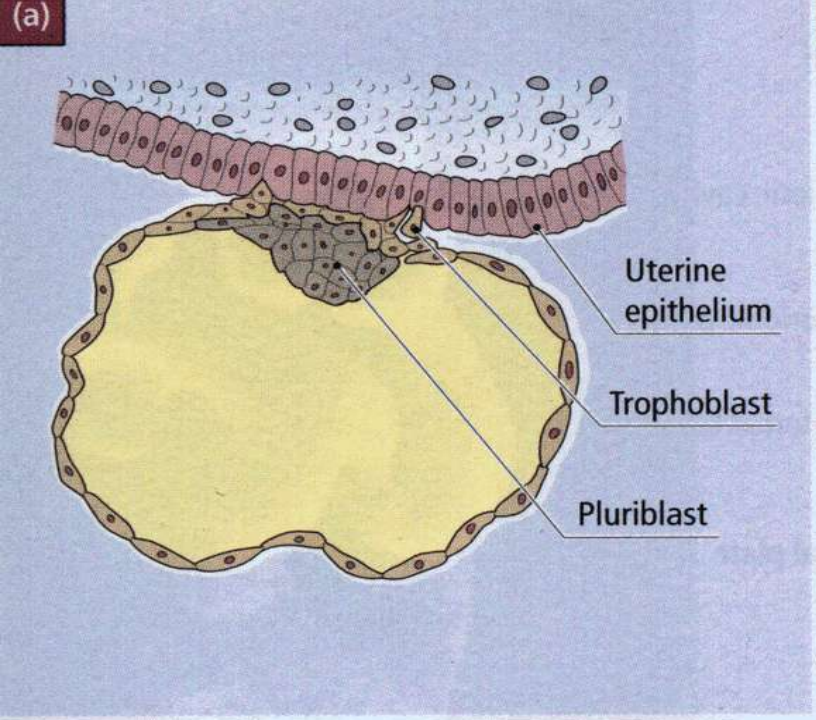
Implantation – the trophoblast of the hatched blastocyst invades the uterine epithelium





Pic: Johnson Essential Reproduction.

The trophoblast develops into a placenta



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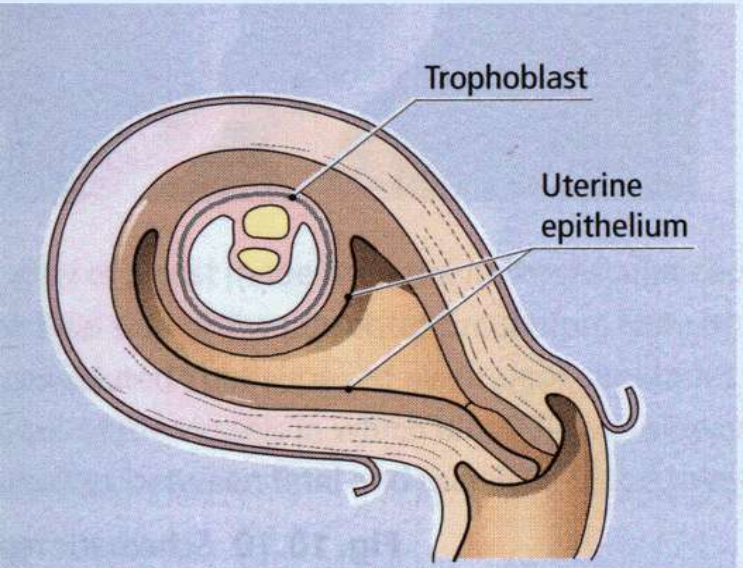
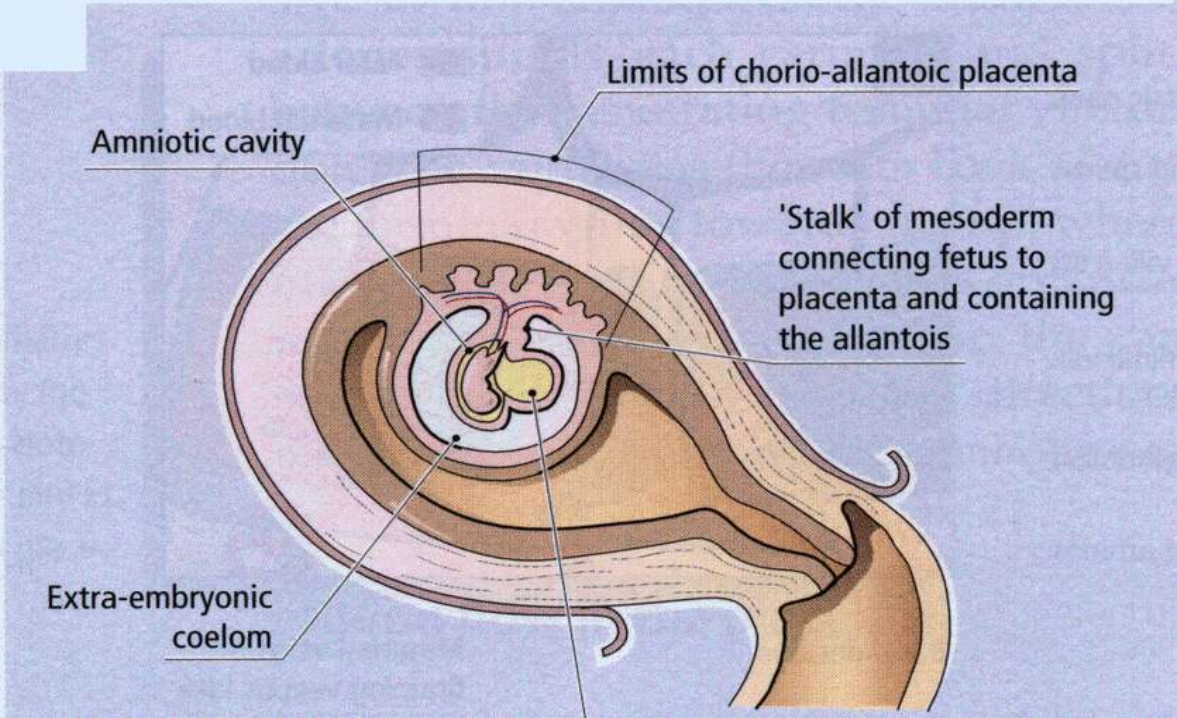
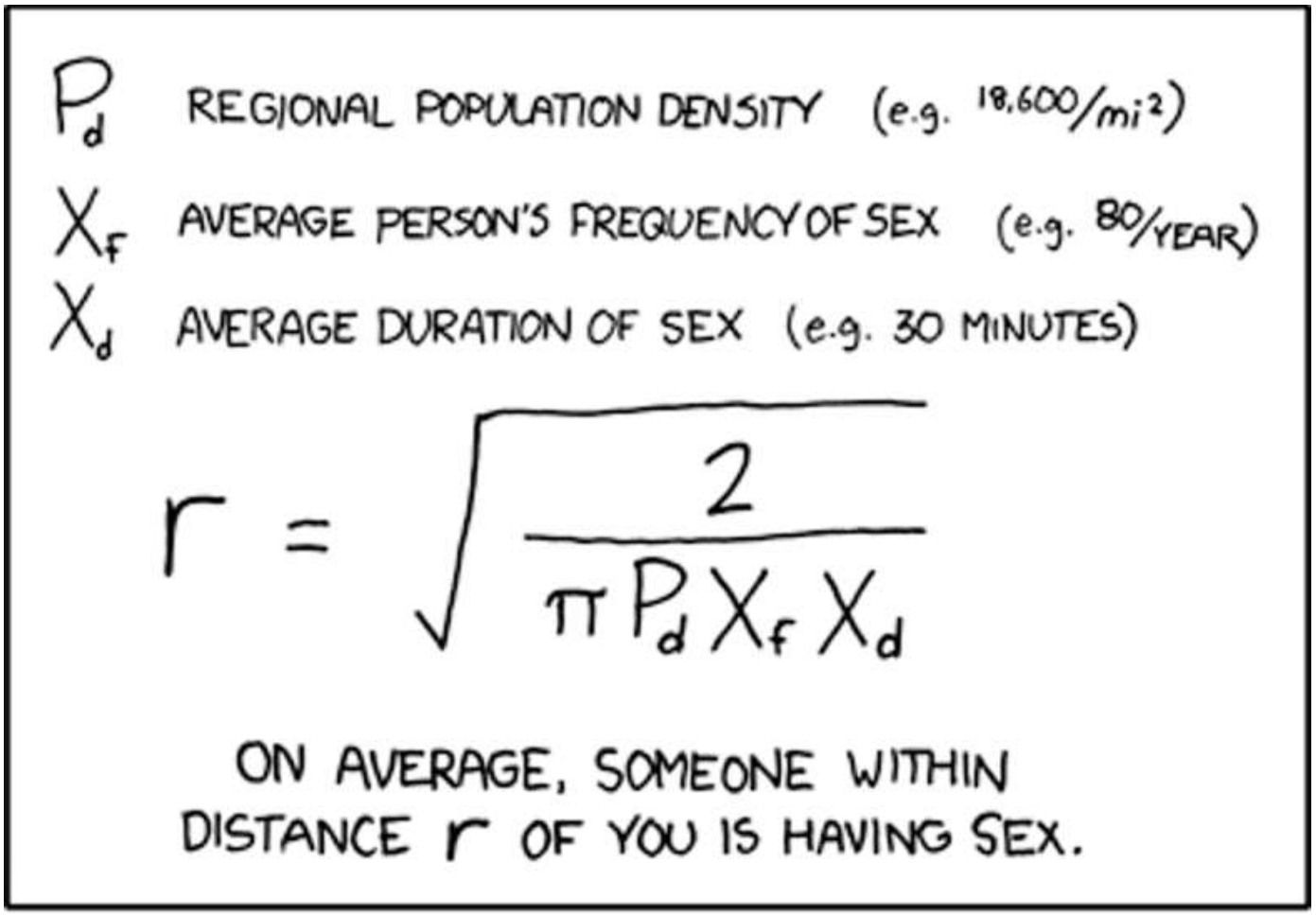




A final thought for the mathematically inclined



Source: xkcd

A WEBCOMIC OF ROMANCE, SARCASM, MATH, AND LANGUAGE.