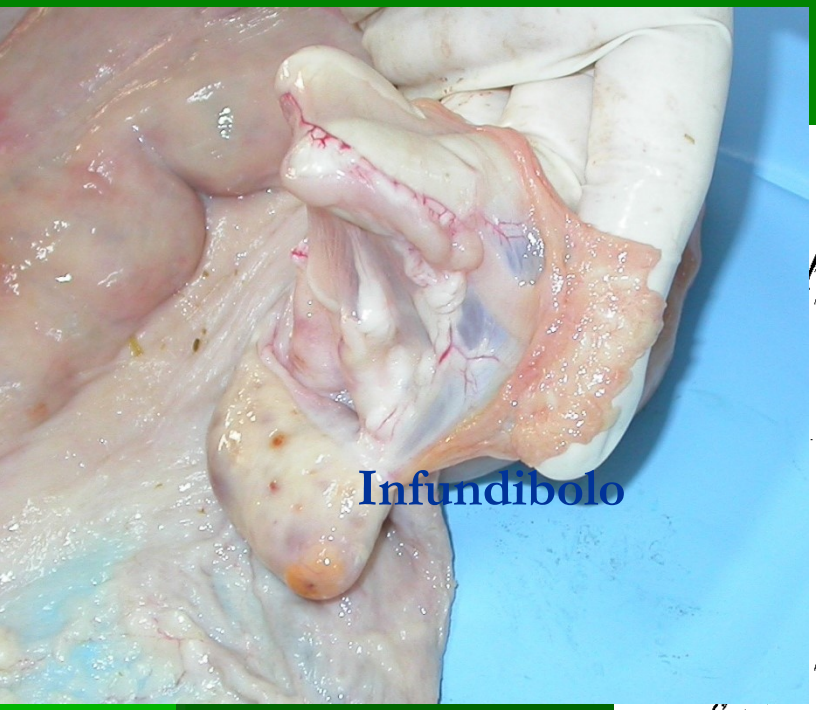
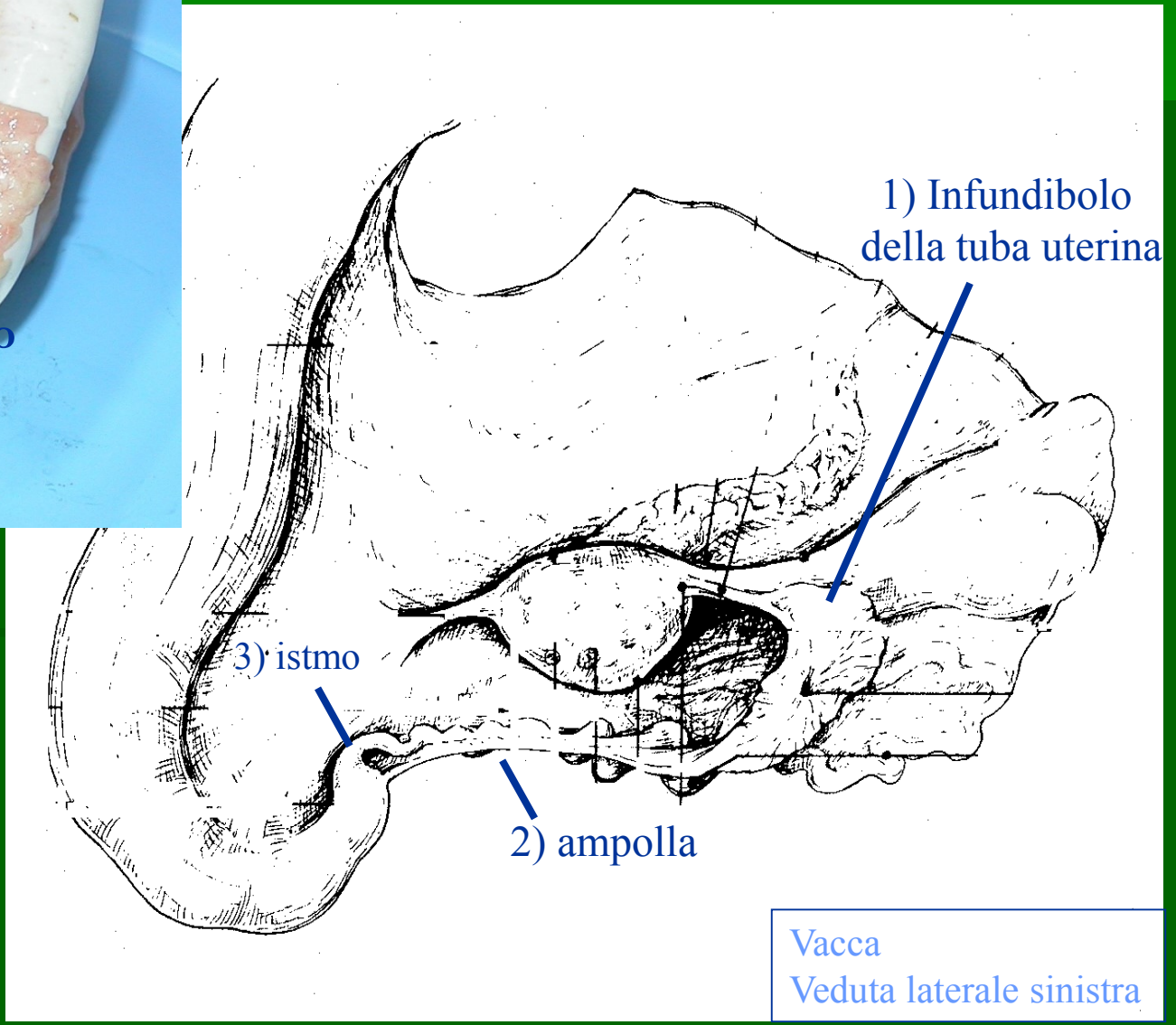
TUBE

TUBA UTERINA

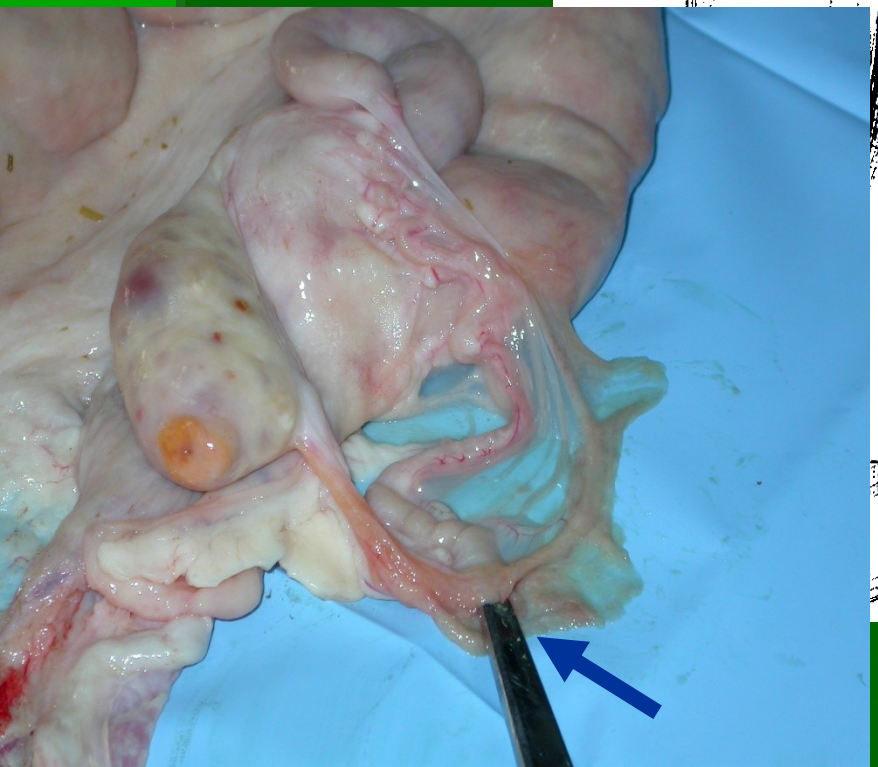


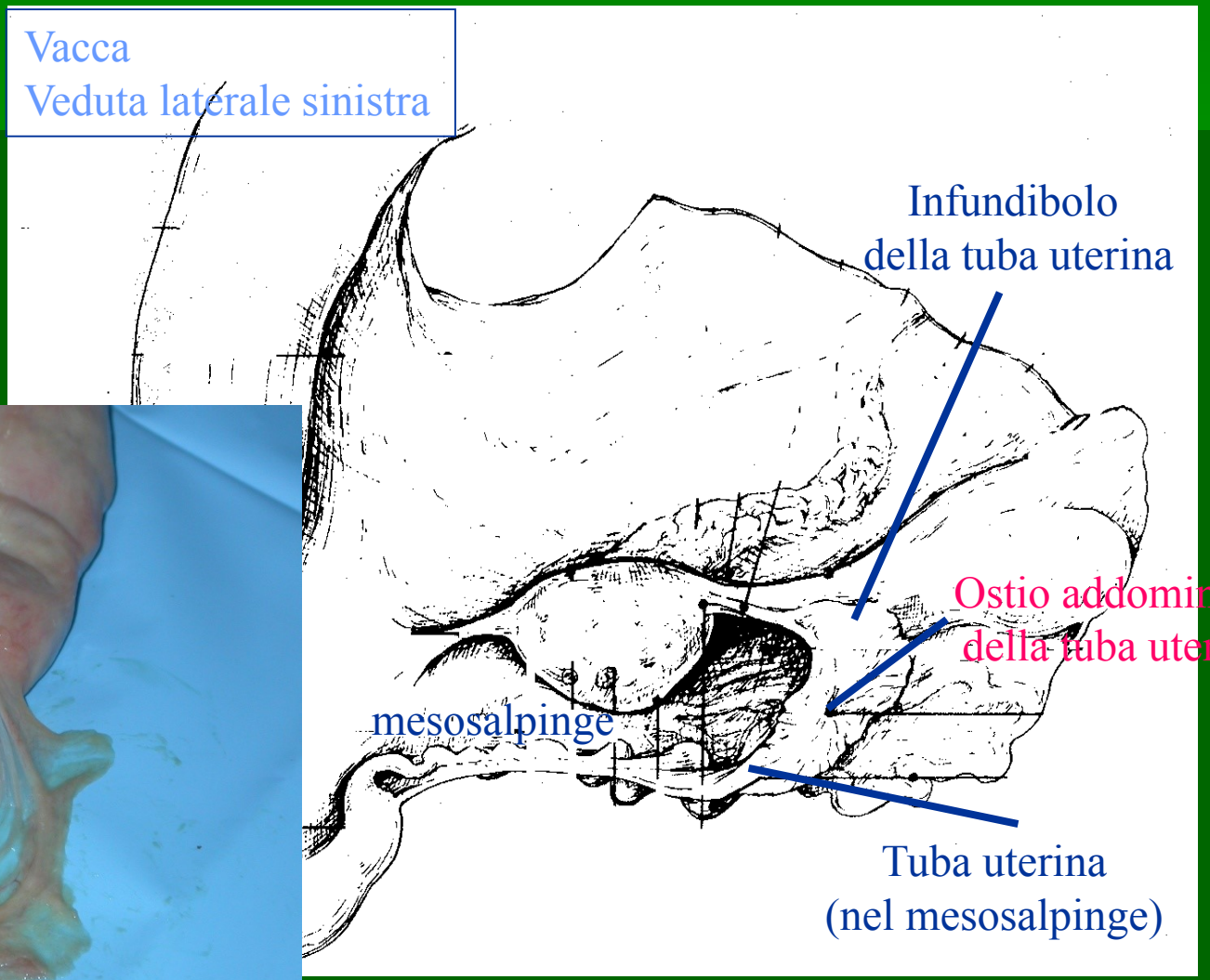


Vacca
Veduta laterale sinistra

TUBA UTERINA

Vacca
Veduta laterale sinistra





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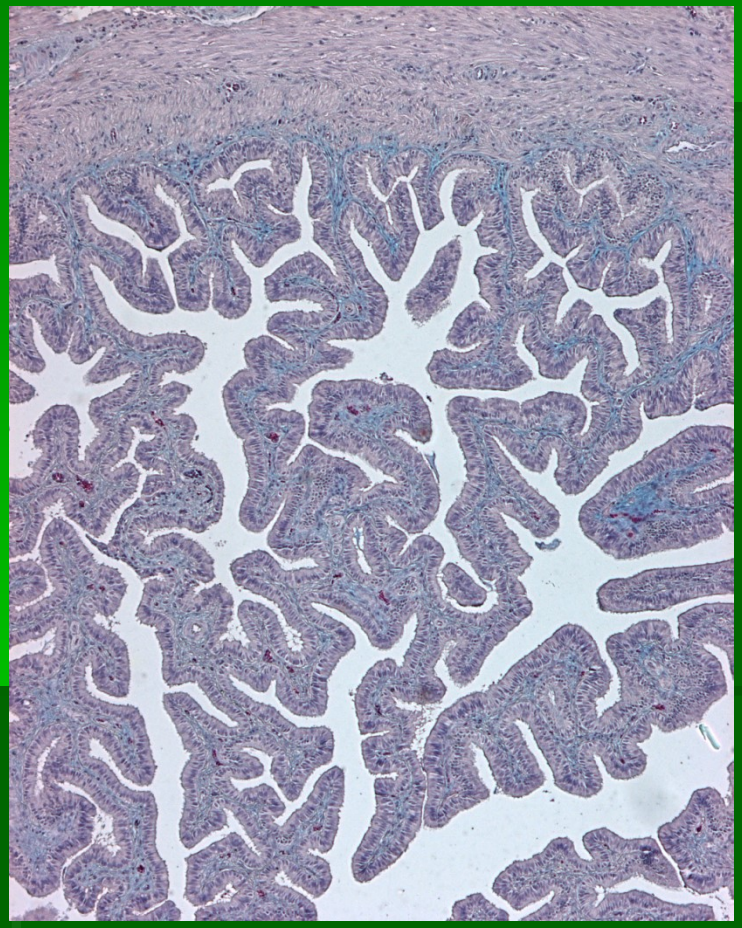

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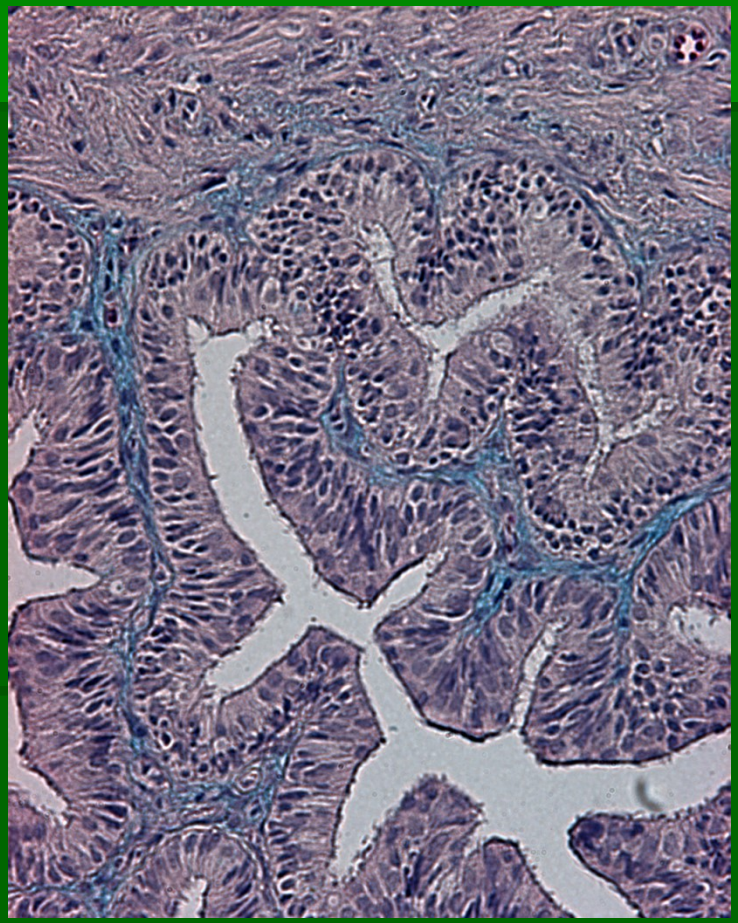
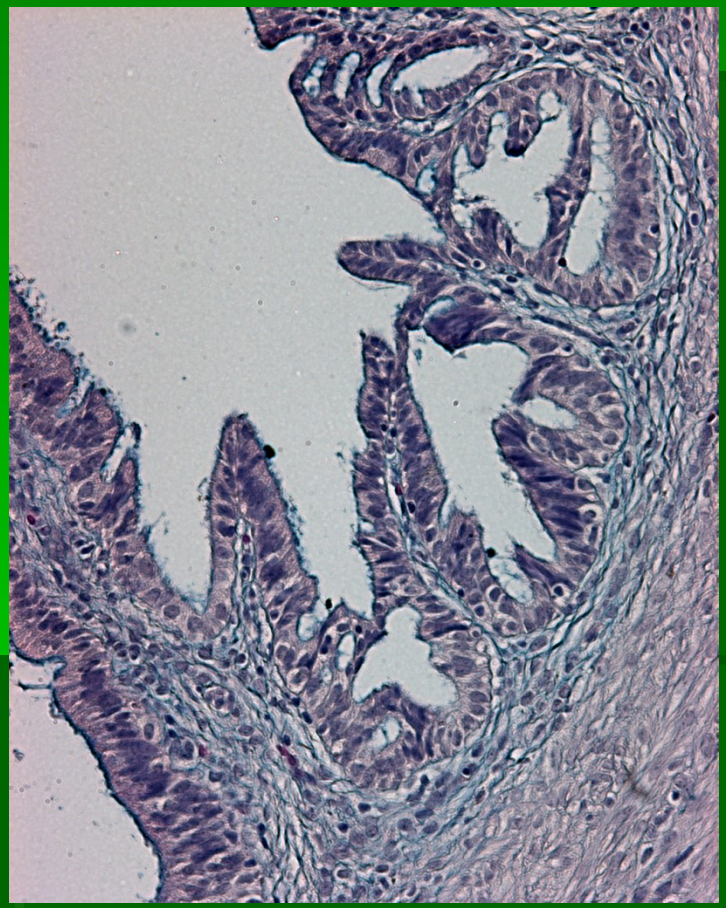


20 X

ISTMO



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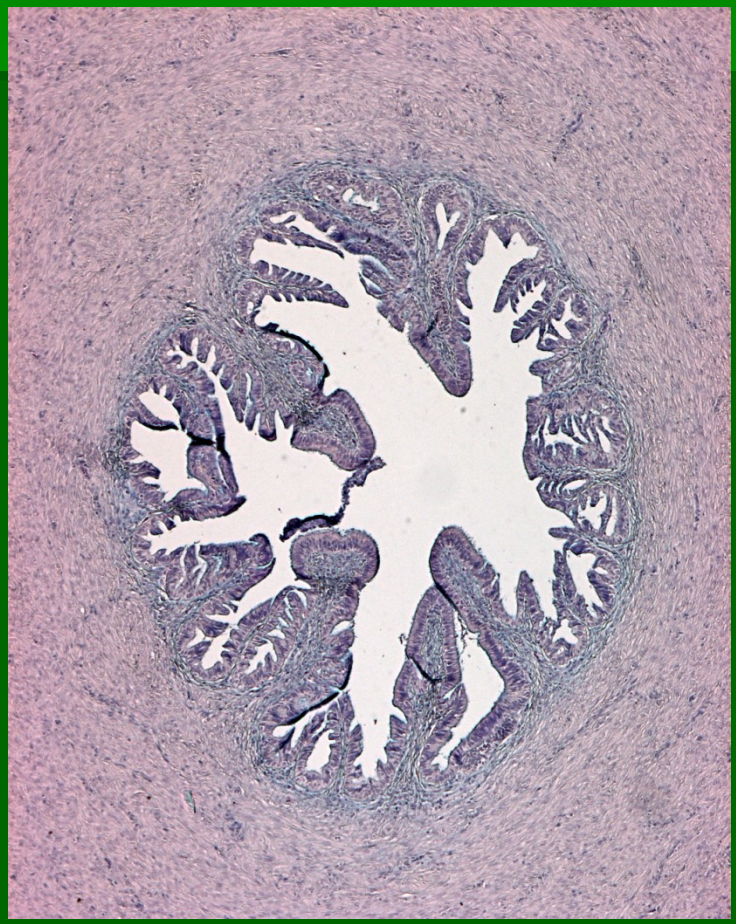

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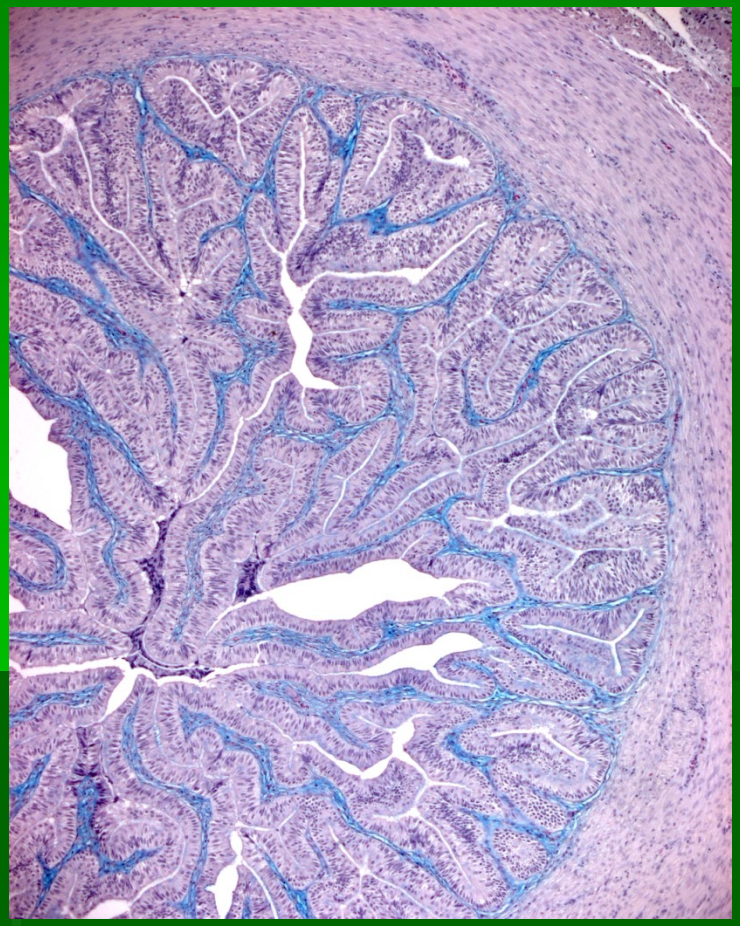
GIUNZIONE



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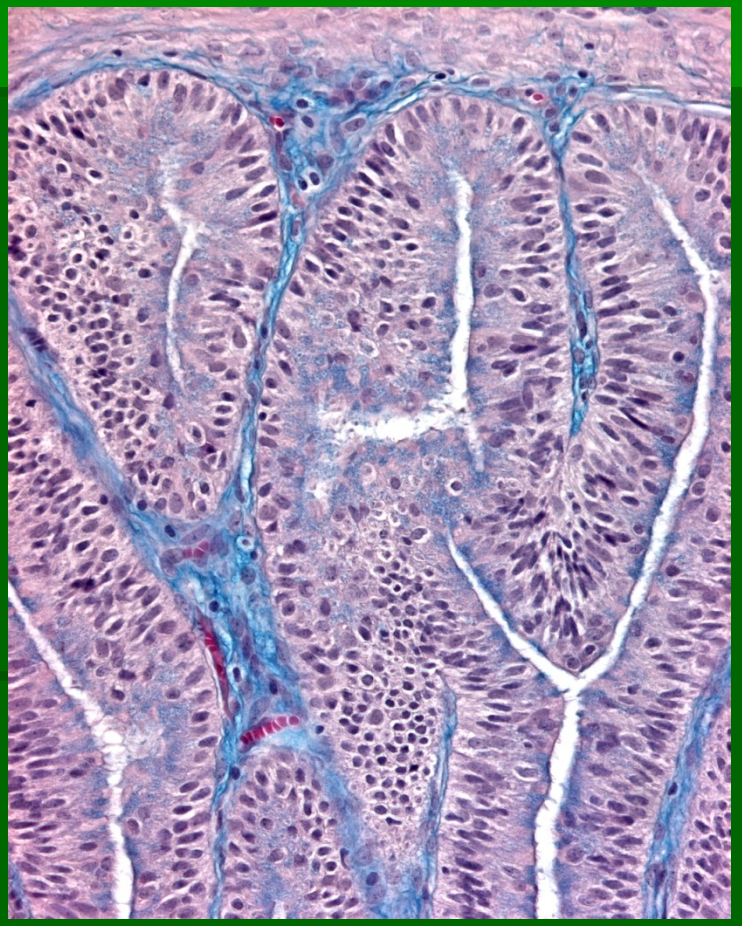
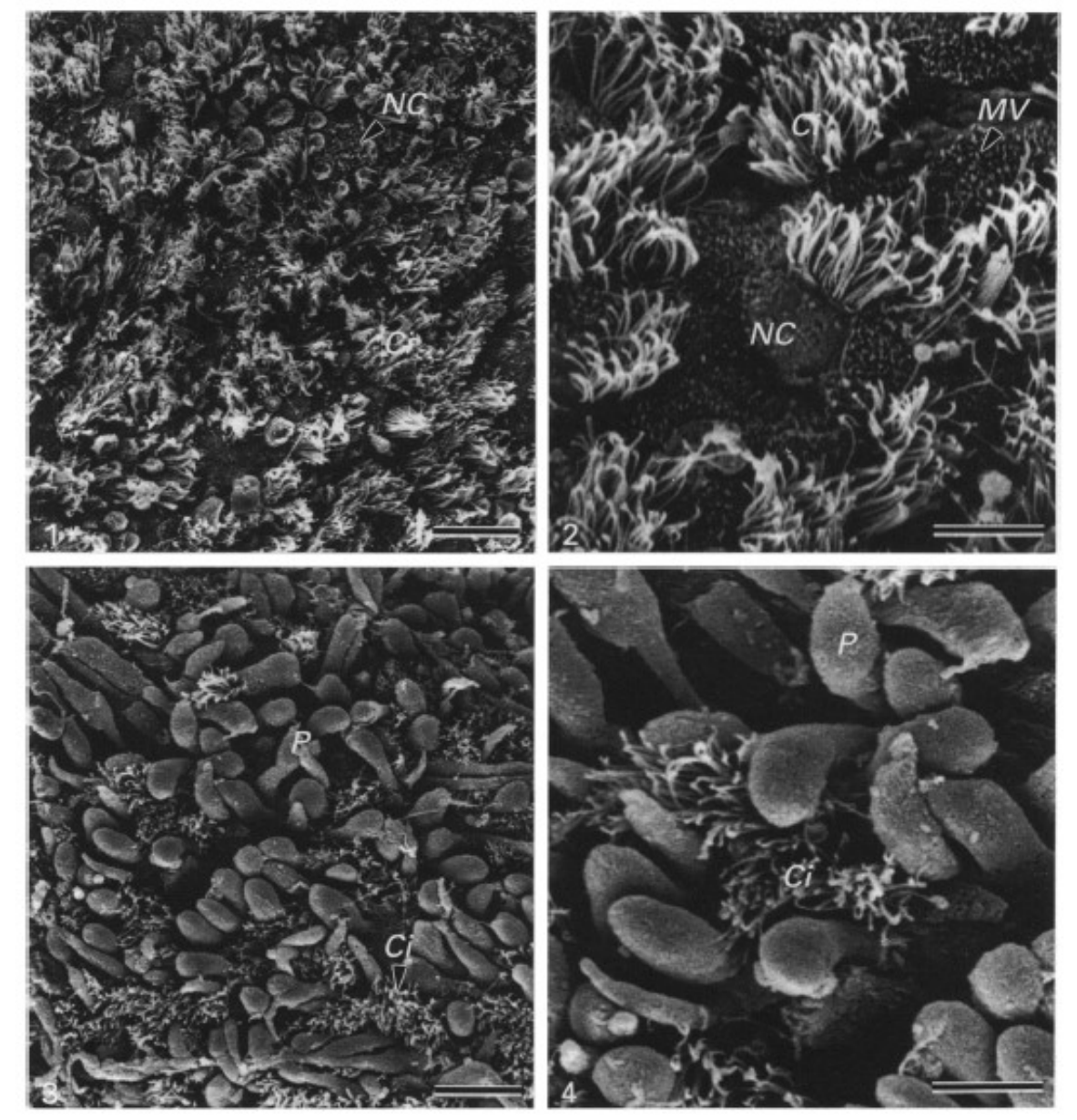


20 X

FIMBRIA



FASE FOLLICOLARE

FASE LUTEINICA

FIMBRIA

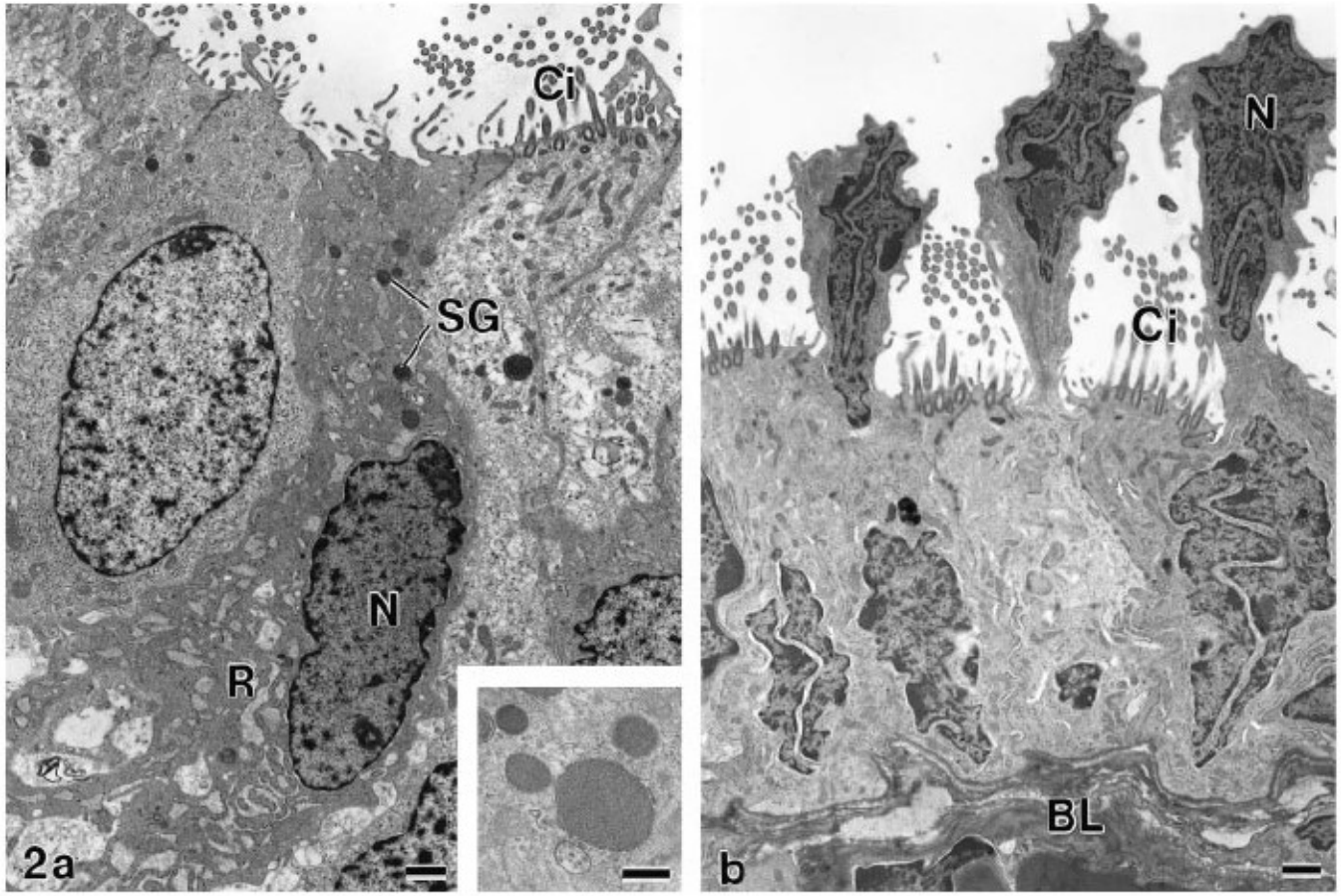
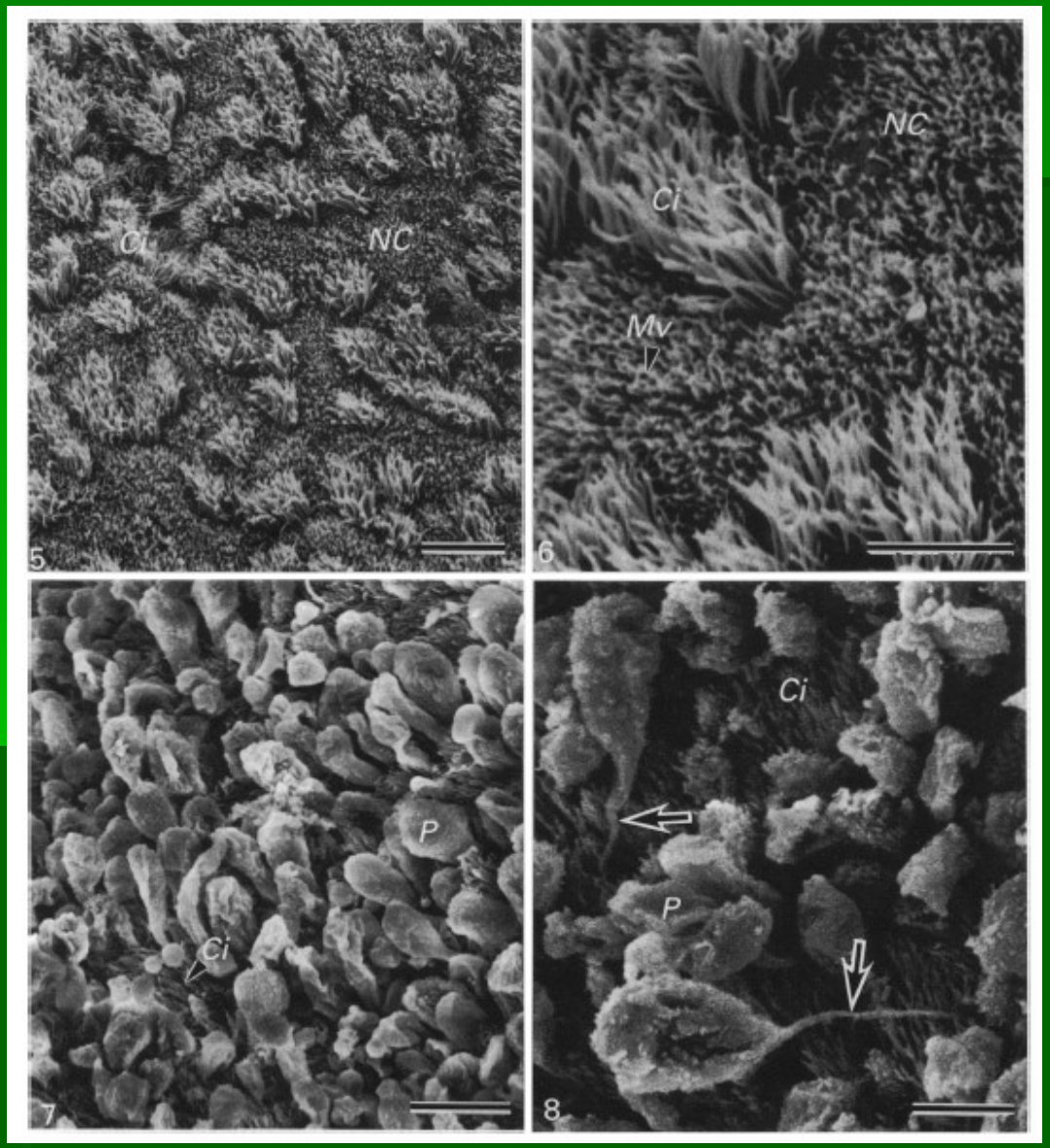


Fig. 2. Fimbrial epithelial cells of goat oviducts at the follicular (*a*) and luteal (*b*) phases of the oestrous cycle. (*a*) The fimbrial secretory cells at the follicular phase have secretory granules (SG) and extensive rough endoplasmic reticulum (R) in their cytoplasm. Inset: Most of the secretory granules are small in size and have an electron-dense homogeneous matrix. (*b*) The nonciliated cells display large cytoplasmic protrusions, usually containing the nucleus (N). BL, basal lamina; Ci, cilia. Bars, 1 μm (in inset, 0.5 μm).

FASE FOLLICOLARE

FASE LUTEINICA

AMPOLLA



FASE FOLLICOLARE

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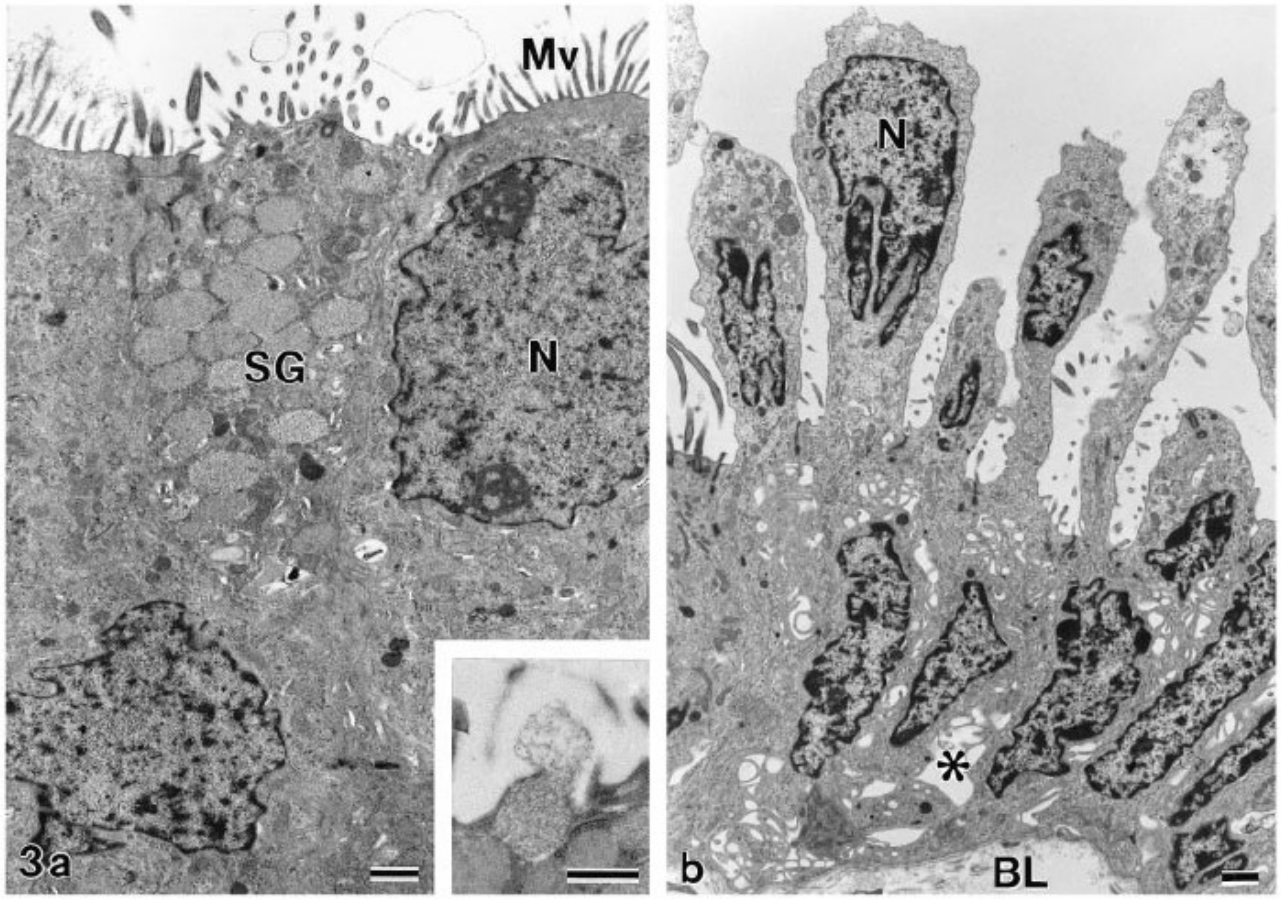
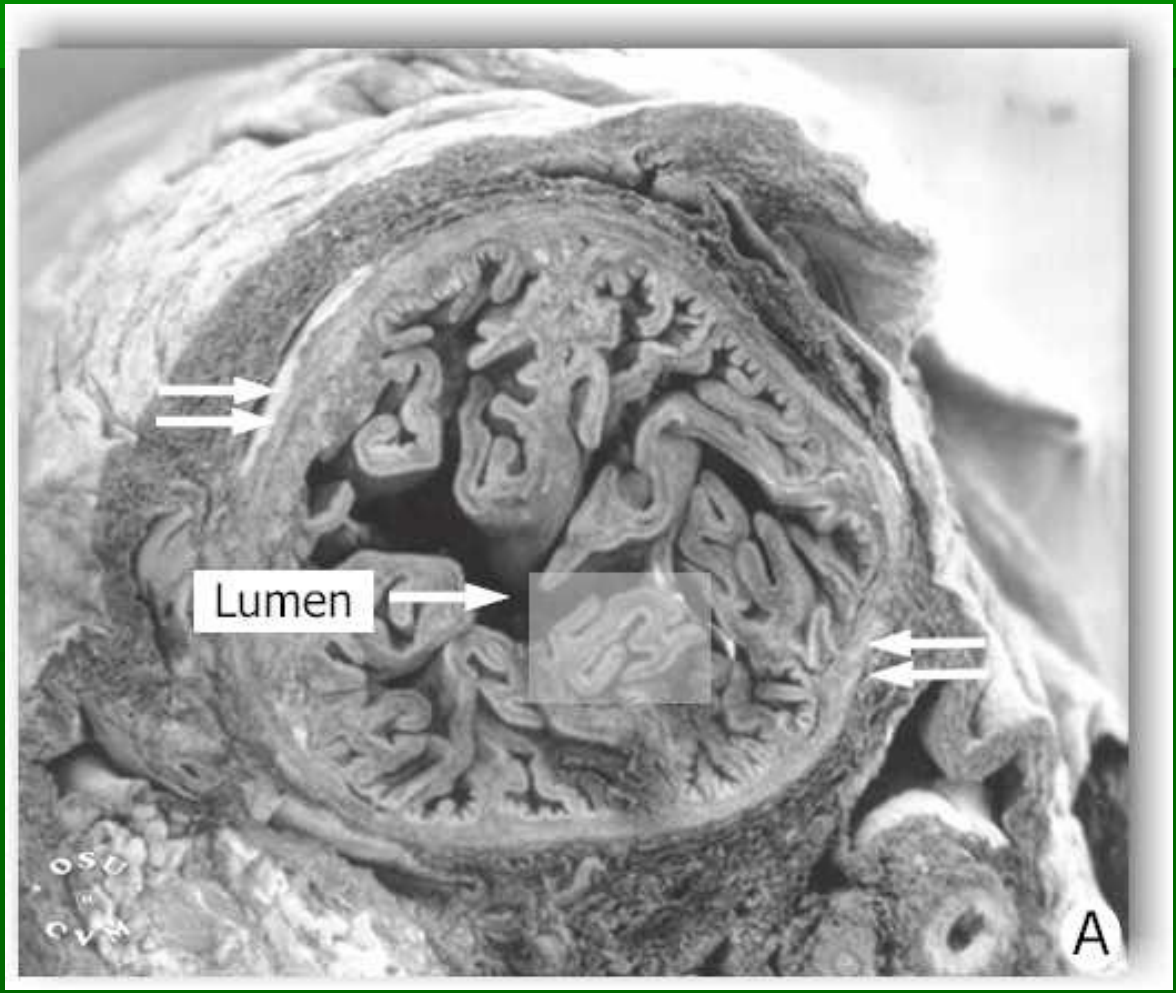


Fig. 3. Ampullary epithelial cells of goat oviducts at the follicular (*a*) and luteal (*b*) phases of the oestrous cycle. (*a*) The ampullary secretory cells at the follicular phase have numerous secretory granules (SG) in the supranuclear cytoplasm. Inset: This figure suggests the exocytosis of a secretory granule. (*b*) The secretory cells display large, long cytoplasmic protrusions, often containing the nucleus and secretory granules. A large intercellular space (asterisk) and interdigitations between the epithelial cells are seen. BL, basal lamina; Mv, microvilli. Bars, 1 μm (in inset, 0.5 μm).

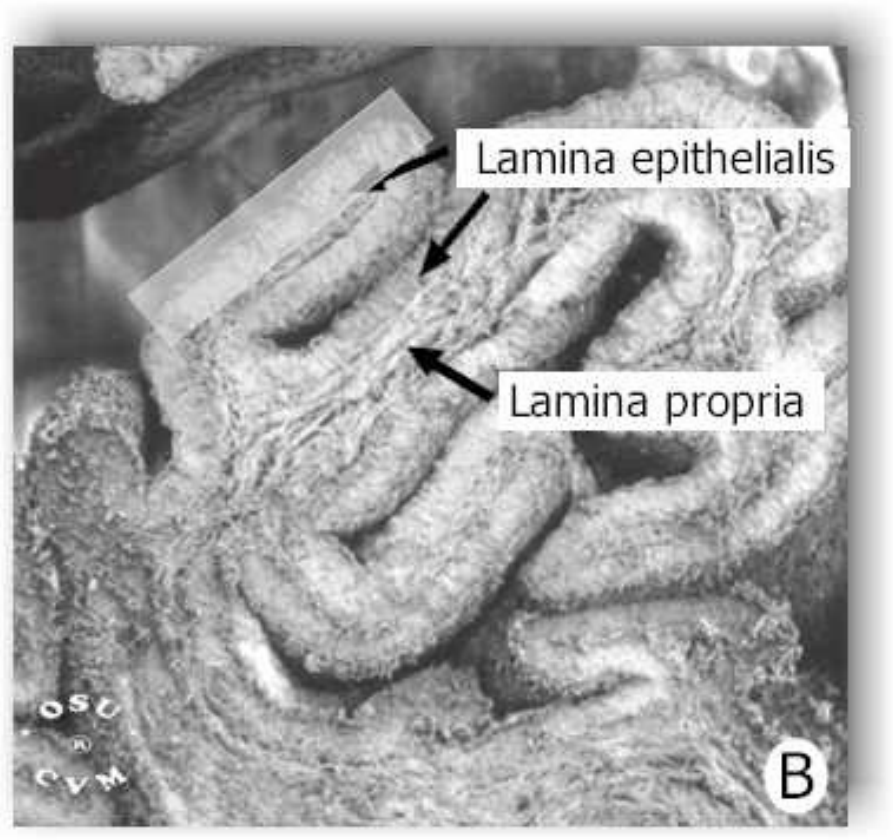
FASE FOLLICOLARE

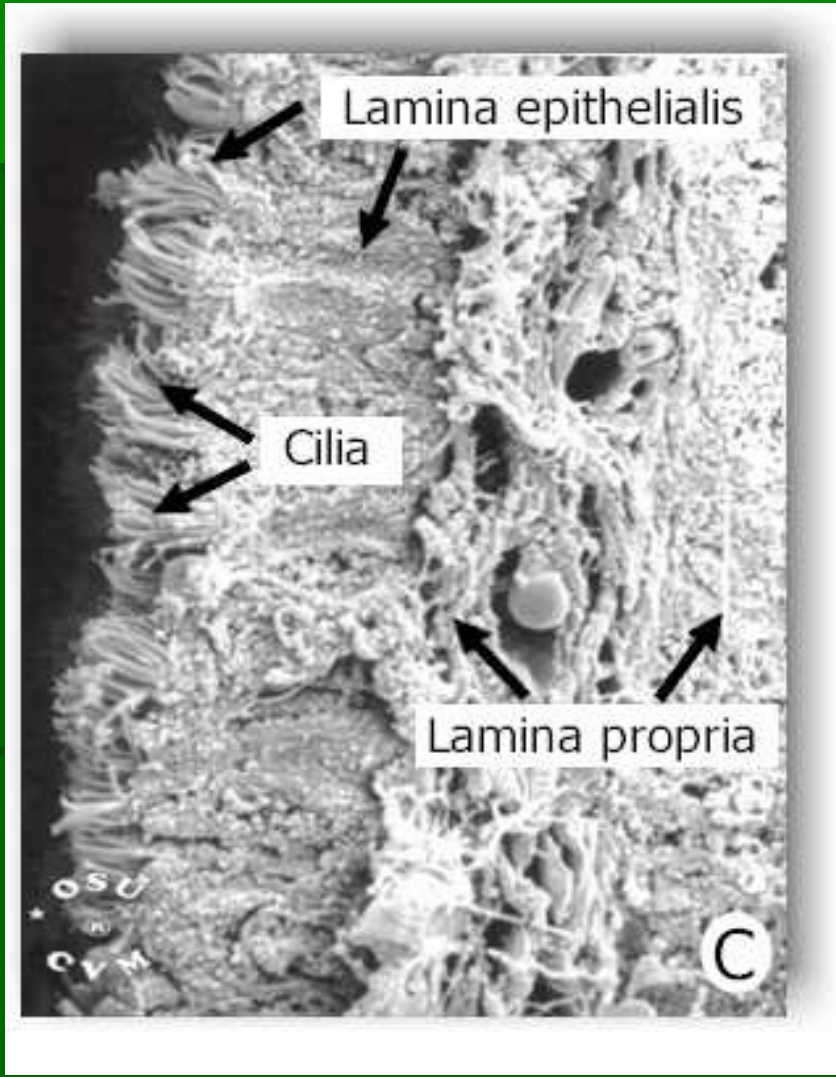
FASE LUTEINICA

AMPOLLA

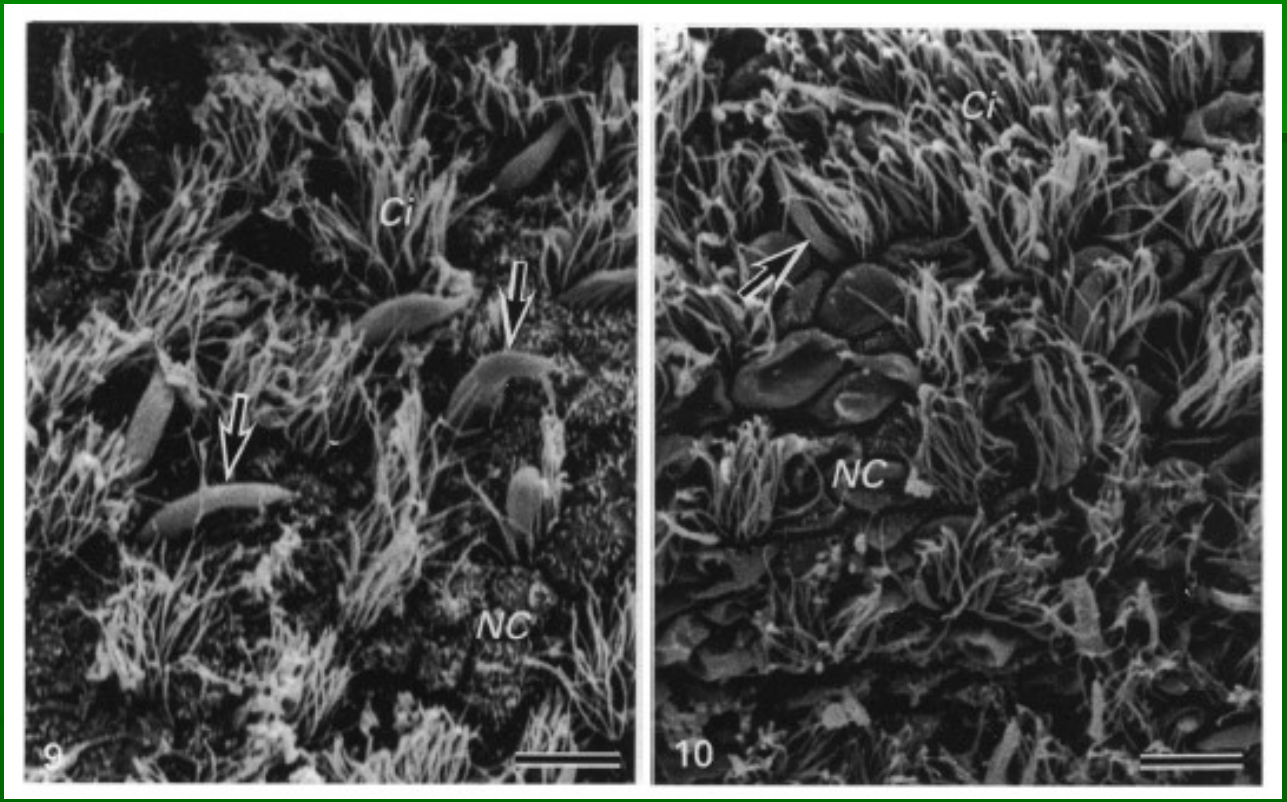


AMPOLLA


Lamina epithelialis
Lamina propria
B


Lamina epithelialis
Cilia
Lamina propria
C

ISTMO



FASE FOLLICOLARE

FASE LUTEINICA

ISTMO

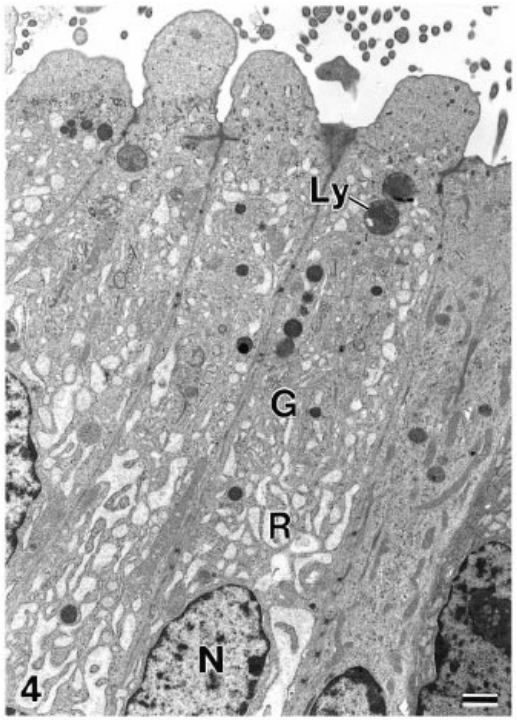


Fig. 4. Isthmic epithelial cells of goat oviducts at the follicular phase of the oestrous cycle. The nonciliated cells have extensive rough endoplasmic reticulum (R) and lysosome-like bodies (Ly). G, Golgi apparatus; N, nucleus. Bar, 1 µm.

FASE FOLLICOLARE

MICROCHIRURGIA

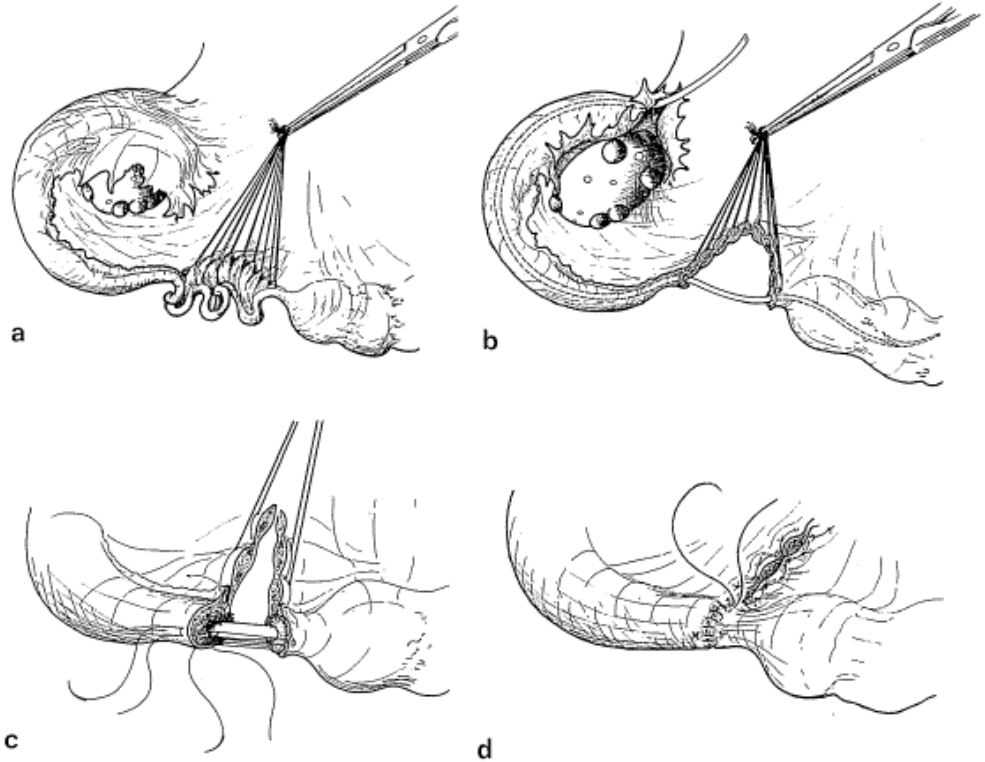


Figure 2. Tubal reconstructive surgery in the domestic pig to examine the influence upon the normality of fertilisation of resecting most of the isthmus followed by end-to-end anastomosis (modified from Hunter and Léglise [2]).

MICROCHIRURGIA

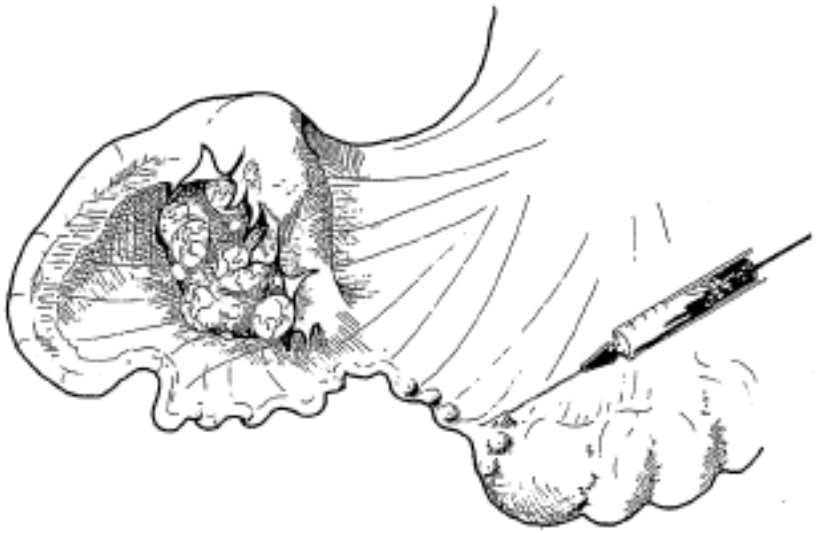


Figure 3. Semi-diagrammatic illustration of one Fallopian tube, proximal uterine horn and portion of a pig ovary bearing pre-ovulatory follicles. Microdroplets of a solution of progesterone in oil injected beneath the serosal layer surrounding the distal isthmus and utero-tubal junction resulted in a 33% incidence of polyspermy in the eggs subsequently recovered from this tube [36].

FLUIDO TUBARICO

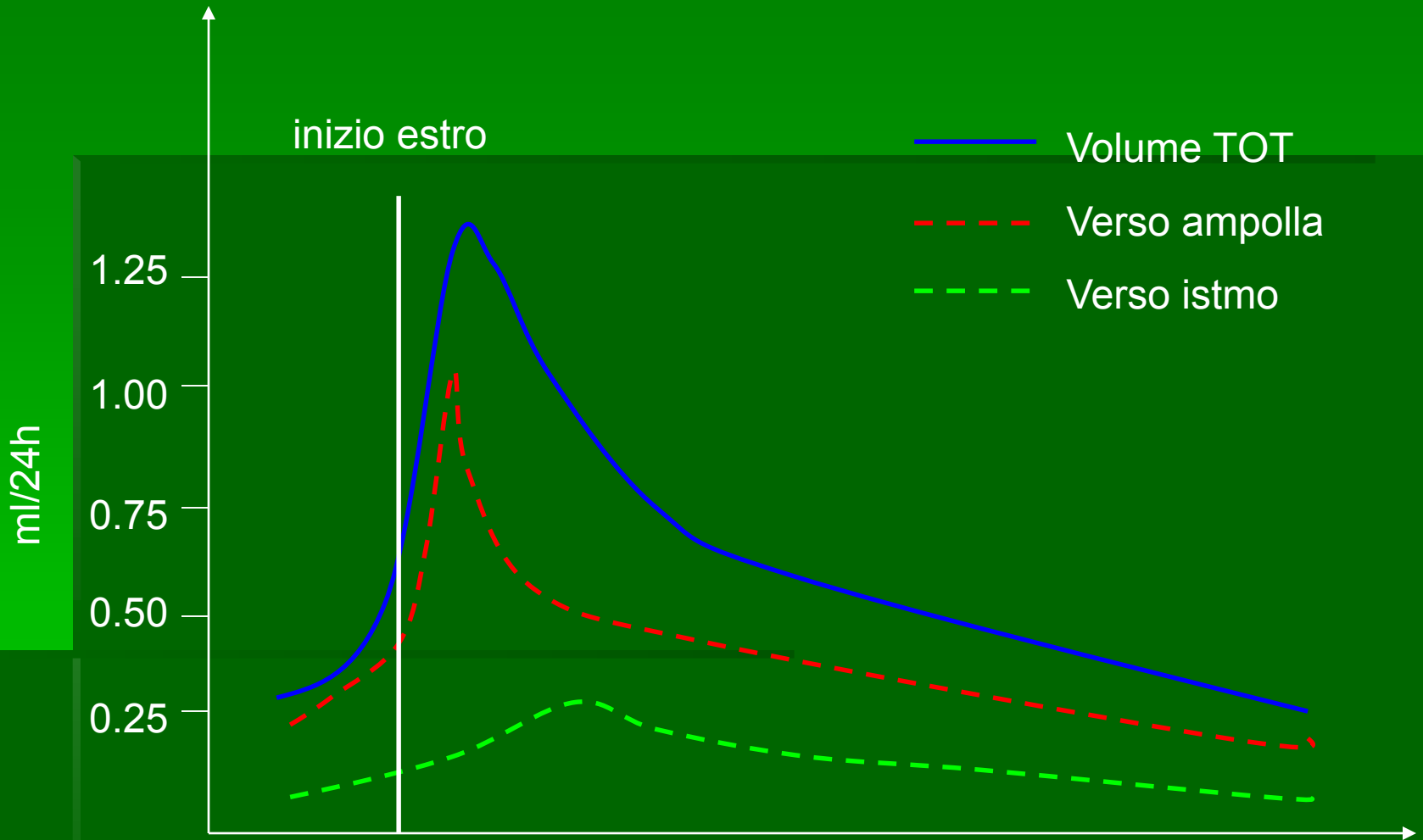
- IL VOLUME E LA COMPOSIZIONE DEL FT VARIANO A SECONDA DEL QUADRO ENDOCRINO.
- COSTITUISCE L'AMBIENTE NEL QUALE AVVIENE LA FECONDAZIONE
- RIFLESSI PRATICI: terreni IVF

  trattamenti anticoncezionali

Volume FT

- Il FT deriva:
- **da un processo di trasudazione selettiva dai vasi;**
- **da un processo di secrezione attiva delle cellule tubariche;**
- dal fluido follicolare rilasciato con l'ovulazione;
- dal fluido peritoneale (maggiormente in animali senza borsa ovarica);
- dal fluido uterino refluito.

Volume FT


inizio estro
Volume TOT
Verso ampolla
Verso istmo
1.25
1.00
0.75
0.50
0.25
ml/24h

COMPOSIZIONE FT

- CARATTERISTICHE CHIMICO-FISICHE:

- 302-310 mOsm/l
- pH 7.3 - 8.2

Differenze regionali

COMPOSIZIONE FT

- PROTEINE ED AA: mediamente la concentrazione proteica è inferiore a quella del sangue (passaggio selettivo).

  Variazioni inter- ed intra- individuali e specifiche.

AMINOACIDI

Table 5. Amino acid concentrations in tubal fluids of various species (μM/mL).

Amino Acid	Mouse	Rabbit	Rabbit	Ewe	Ewe	Pig	Cow	Mare
3-methyl histidine	0.000	0.020	ND	0.019	ND	0.000	0.017	ND
Alanine	0.506	0.475	0.469	0.241	0.440	0.171	1.263	0.140
Arginine	0.023	0.024	0.064	0.048	0.140	0.059	0.202	0.031
Asparagine	0.014	0.036	ND	0.016	0.020	0.011	0.012	ND
Aspartic acid	0.215	0.025	0.024	0.021	0.120	0.004	0.061	0.022
Citrulline	0.020	0.023	ND	0.035	A	0.015	0.048	ND
Cystine	0.002	0.015	0.015	0.0008	B	0.001	0.001	0.003
Glutamic acid	0.497	0.211	0.192	0.047	0.200	0.005	0.361	0.057
Glutamine	0.347	0.272	ND	0.058	0.190	0.034	0.143	ND
Glycine	0.586	2.889	2.766	2.288	2.300	0.875	2.601	0.263
Histidine	0.021	0.070	0.067	0.031	0.070	0.019	0.152	0.020
Hypotaurine	0.141	0.158	ND	0.350	0.350	0.196	0.155	ND
Isoleucine	0.024	0.053	0.069	0.036	0.130	0.024	0.179	0.025
Leucine	0.043	0.099	0.129	0.083	0.250	0.033	0.352	0.053
Lysine	0.093	0.060	0.165	0.090	0.210	0.066	0.417	0.053
Methionine	0.029	0.032	0.022	0.014	0.050	0.007	0.075	0.014
Ornithine	0.028	0.015	ND	0.022	B	0.018	0.098	ND
Phenylalanine	0.033	0.051	0.065	0.030	0.180	0.013	0.154	0.026
Proline	0.141	0.102	C	0.047	0.300	0.001	0.200	0.048
Serine	0.136	0.201	0.318	0.024	0.040	0.050	0.121	0.051
Taurine	2.000	0.074	0.123	0.047	0.040	0.236	0.091	ND
Threonine	0.187	0.154	0.125	0.013	A	0.020	0.081	0.038
Tyrosine	0.032	0.066	0.079	0.032	0.150	0.014	0.123	0.041
Tryptophan	0.001	0.008	Undetectable	0.002	0.070	0.000	0.016	ND
Valine	0.104	0.169	0.172	0.079	0.250	0.036	0.250	0.041
References	Guerin *et al.*, 1995b	Guerin *et al.*, 1995b	Iritani *et al.*, 1971	Guerin *et al.*, 1995b	Moses *et al.*, 1997	Guerin *et al.*, 1995b	Guerin *et al.*, 1995b	Engle *et al.*, 1984

ND: not determined
A: Citrulline + Threonine: 0.140
B: Cystine + Ornithine: 0.050
C: Cystine + Proline: 0.086

FATTORI DI CRESCITA

Table 6. Growth factors present in tubal fluids of various species.

Growth Factor	Human	Bovine	Ovine	Porcine	Baboon	Mare
Activin β A		X				
Amphiregulin				X		
Acidic FGF		X				
Basic FGF		X	X			
EGF	X	X	N/D	X	X	
EGFR	X	X		X	X	
HB-EGF				N/D		
GM-CSF	X					
GM-CSF αR	X					
GM-CSF βR	X					
IGF 2R		X				
IGFBP1	X	N/D				
IGFBP2	X	X	N/D			
IGFBP3	X	X	X			
IGFBP4	X	X	X			
IGFBP5		X				
IGFBP6		N/D				
IGF-I	X	X	X	X		
IGF-IR	X	X	X			
IGF-II		X	X	X		
Insulin R		X	X			
NGF			N/D			
PDGF		X				X
TGF α	X	X	X	X	X	
TGF β1			X			

References. **Humans**: Chegini *et al*., 1994; Zhao and Chegini, 1994; Pfeifer and Chegini, 1994; Smotrich *et al*., 1996; Adachi *et al*., 1995. **Bovine**: Viuff *et al*., 1995; Makarevich and Sirotkin, 1997; Gandolfi *et al*., 1995 ; Xia *et al*., 1996 ; Winger *et al*., 1997; Modina *et al*., 1997. **Ovine**: Watson *et al*., 1994; Stevenson and Wathes, 1996. **Porcine**: Wiseman *et al*., 1992; Swanchara *et al*., 1995; Kennedy *et al*., 1994; Wollenhaupt *et al*., 1997. **Baboon**: Schell *et al*., 1994. **Mare**: Eriksen *et al*., 1994.

FGF: fibroblast growth factor; EGF: epidermal growth factor; EGFR: epidermal growth factor receptor; HB-EGF: heparin-binding epidermal growth factor; GM-CSF: granulocyte macrophage colony stimulating factor; IGF: insulin-like growth factor; IGFBP: insulin-like growth factor binding protein; PDGF: platelet derived growth factor; TGF: transforming growth factor; N/D: not detected.

COMPOSIZIONE FT

- ELETTROLITI: Na^+ e Cl^- i principali. Ca^{2+}, K^+ sono in concentrazione inferiore rispetto al sangue.

  $HCO3^-$: la sua concentrazione aumenta per effetto degli estrogeni.

ELETTROLITI

Table 3. Concentrations of ions in the uterine tubal fluid of various species collected from ampulla, isthmus, or the whole tube (mEq/L).

	Cow		Cow	Ewe		Rabbit	Rabbit	Human	Human	Human	Mare
	Ampulla	Isthmus	Whole	Ampulla	Isthmus	Whole	Whole	Whole	Whole	Whole	Whole
Na	140.9	159.3	86.1	135	141	127.8	189.7	130	145	139.5	129.5
Cl			112.7			115.4	332.2	132	119.5	118	
K	4.53	4.24	65.7	8.12	6.9	5.6	16.8	21.1	6.7	8.8	7.9
Ca	1.83	2.64	3.19	7.6	5.96	7.98	2.71	1.13		2.13	2.28
Mg	0.662	0.685		1.18	1.08	0.141	0.473	1.42		0.61	4.59
S								12.3			
P			3.0			0.193		8.69			0.366
Zn						0.099	0.0046				
Bicarbonate							16.55				
References	Grippo *et al*., 1992		Olds and VanDenmark, 1957b	Restall and Wales, 1966; 1968.		David *et al*., 1969	Hamner and Williams, 1965	Borland *et al*., 1977	David *et al*., 1973	Lippes *et al*., 1972	Campbell *et al*., 1979

COMPOSIZIONE FT

- SUBSTRATI ENERGETICI: piruvato, lattato, glucosio, glicogeno. Aumentano per azione degli estrogeni.

SUBSTRATI ENERGETICI

Table 4. Concentration of energy substrates in uterine tubal fluid of some species (mM).

	Mouse	Ewe	Sow		Human	Cow	Mare
			Ampulla	Isthmus			
Glucose	3.4	1.57-1.76	0.25-097	0.17-1.65	0.53	0.02-0.04	2.84-5.92
Lactate	4.7	1.67-2.51	3.86-6.83	4.93-6.48	8.58		
Pyruvate	0.37	0.15	0.17-0.22	0.17-0.22	0.17		
References	Gardner and, Leese, 1990	Hamner, 1973	Nichol *et al*., 1992		Dickens *et al*., 1995	Carlson *et al*., 1970	Campbell *et al*., 1979

COMPOSIZIONE FT

- ORMONI: derivano principalmente dal trasudato del sangue. In parte anche da fluido peritoneale, fluido follicolare, cellule della granulosa, embrione (non sappiamo bene in quale misura).

  ESTROGENI, P4, PGs, PRL., …

CIRCOLAZIONE

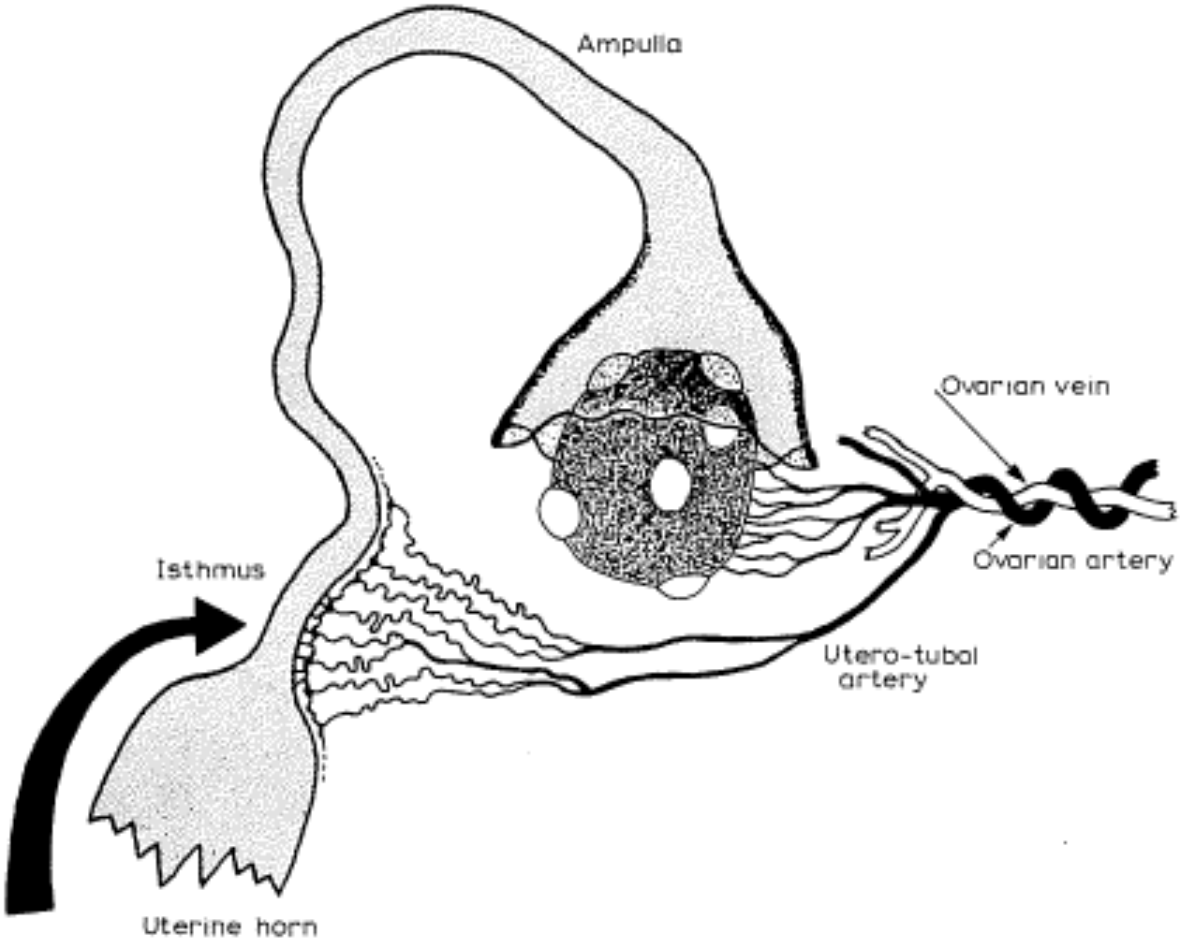


Figure 4. A semi-diagrammatic representation of the arterial blood supply to the ovary and isthmus of the pig Fallopian tube. A portion of the ovarian vein is also shown. A counter-current transfer of follicular hormones was demonstrated from the ovarian vein to the corresponding artery and thus into the utero-tubal branch [37].

GRADIENTI

- Bicarbonato
- Temperatura
- Endocannabinoidi
- Fattori solubili (nutrienti, ioni, …)
- Interazioni con spermatozoo

TRASPORTO OOCITA

- CIGLIA: la loro attività è incrementata a partire dall'ovulazione. Pare che abbiano una certa importanza nel "catturare" gli oociti circondati dal cumulo. Il tempo che passa tra l'ovulazione e l'arrivo dell'oocita nel sito di fecondazione è di pochi minuti (6 – 15 nel coniglio, 30 – 45 nel suino).

TRASPORTO OOCITA

- ATTIVITA' CONTRATTILE MUSCOLATURA LISCIA: dipende da ormoni (e SN). Il trasporto dell'oocita dal sito di fecondazione alla UTJ richiede anche giorni. Non si tratta di un processo lineare.

TRASPORTO SPERMATOZOI

- IL COITO AVVIENE ORE/GIORNI PRIMA DELL'OVULAZIONE.
- In VAGINA: coniglio, ruminanti, primati.
- In UTERO: suino, equino, cane, roditori.

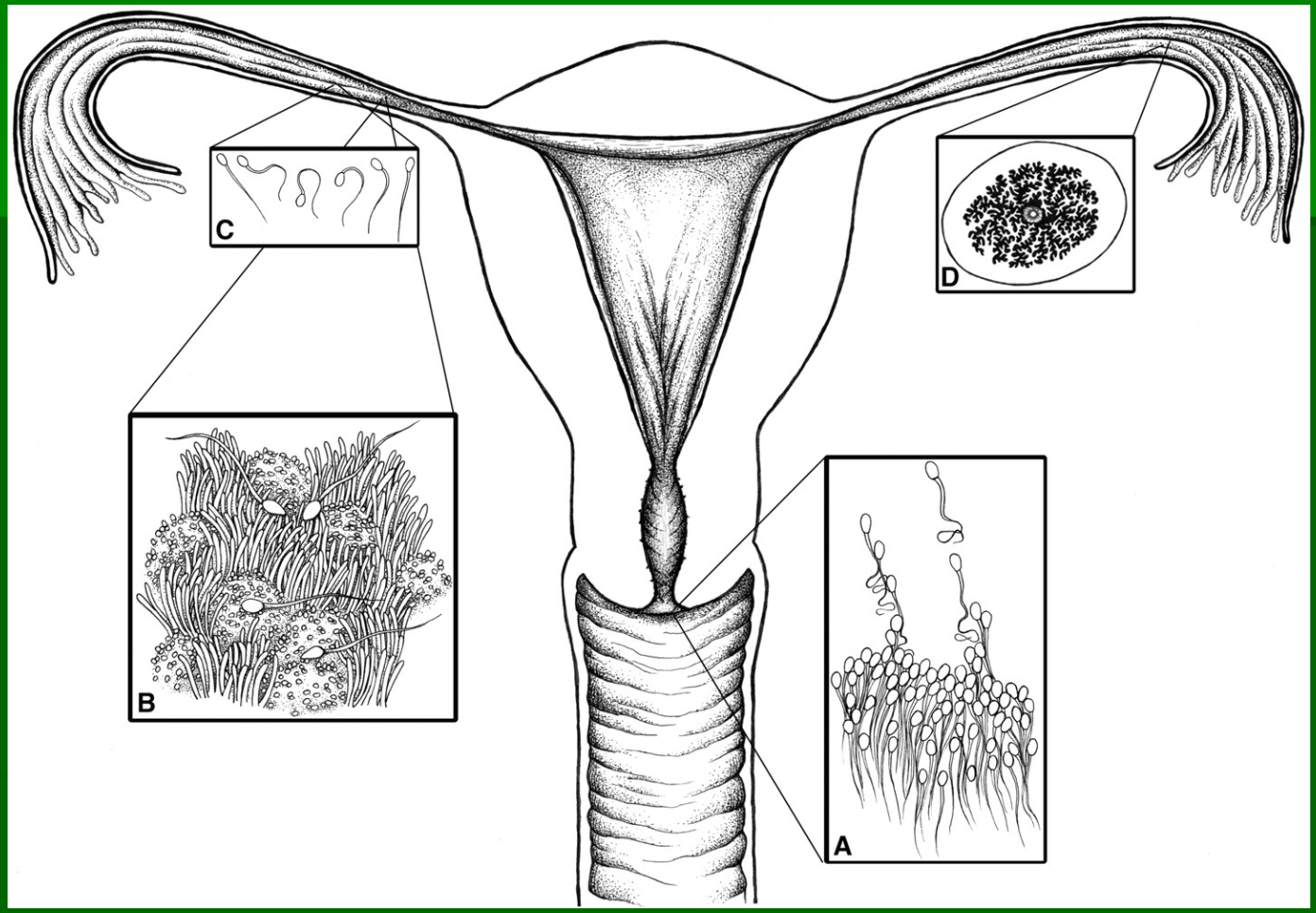
DEPOSIZIONE INTRAVAGINALE

- Il passaggio attraverso la cervice avviene in pochi minuti (<5), grazie alla motilità degli sptz.
- La cripte cervicali funzionano da reservoir temporaneo degli sptz e le interazioni col muco cervicale hanno un ruolo fondamentale.
- La cervice fa passare circa 1/100 degli spermatozoi.

DEPOSIZIONE INTRAVAGINALE

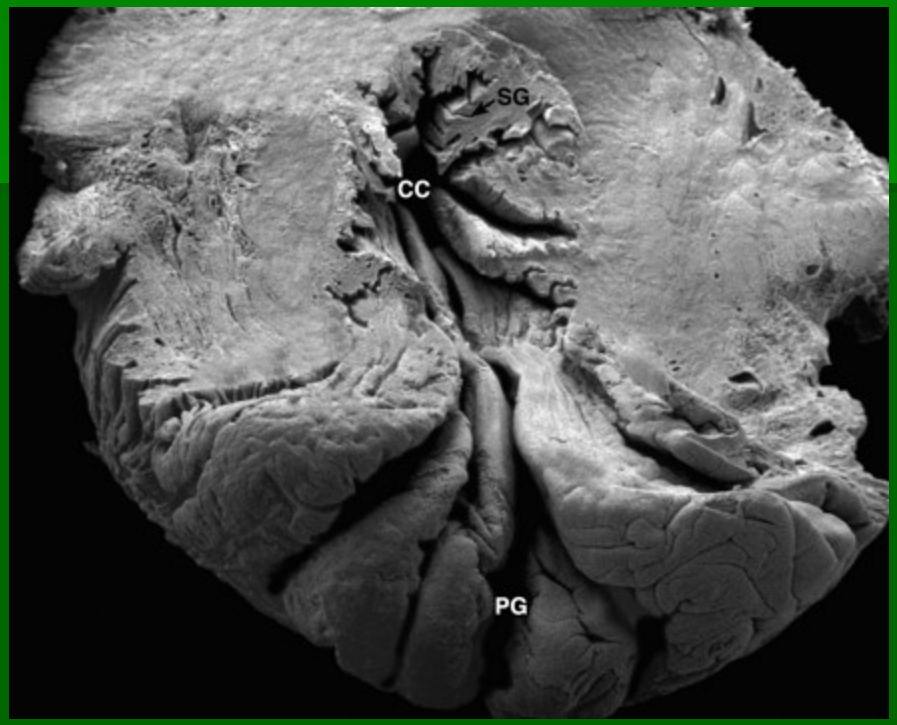
- Inoltre assicura l'allontanamento del PS.
- Il passaggio degli sptz verso le tube è:
- Attivo: motilità
- Passivo: contrazioni miometrio (OX, PGs)
- Sono necessarie almeno 6 – 8 ore.

DONNA



Human female reproductive tract illustrating stages of gamete transport. (**A**) Sperm entering cervical mucus at external os of cervix. The mucus fills the upper half of the inset. (**B**) Sperm interacting with endosalpingeal epithelium in Fallopian tube. (**C**) Hyperactivated motility of sperm in Fallopian tube. (**D**) Oocyte in cumulus within a transverse section of the tubal ampulla.

DONNA

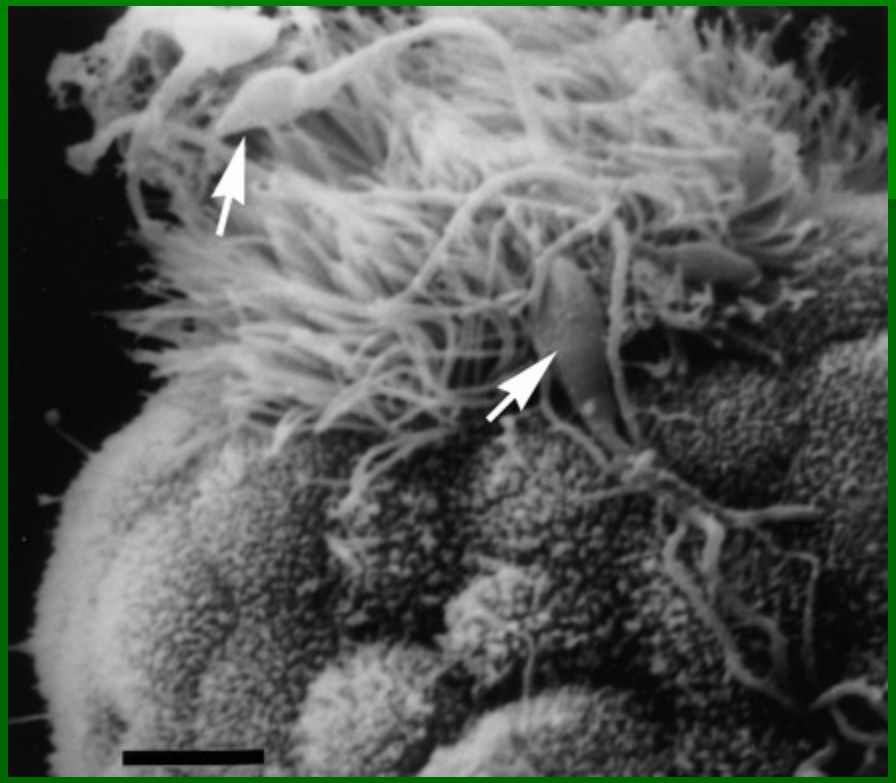


A scanning electron micrograph of the human cervix, illustrating potential passageways for sperm (x67). A portion of the wall has been removed to reveal the architecture of the cervical canal (CC). Large, primary mucosal grooves (PG) can be seen at the external os that extend deep into the cervical canal. Smaller secondary mucosal grooves (SG) branch from the primary grooves. Although the primary grooves appear to form a preferential path for sperm, it is not known whether secondary or even tertiary grooves could end blindly and entrap sperm. Cervical crypts could also trap sperm.

DEPOSIZIONE INTRAUTERINA

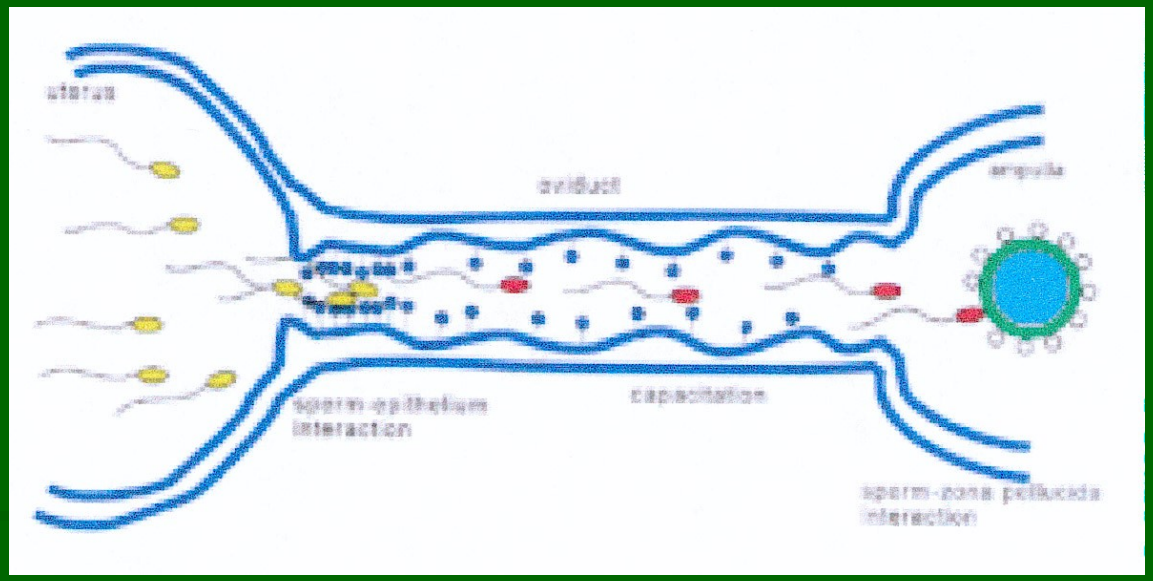
- Punto di selezione è la UTJ.
- Per arrivare alle tube bastano 15 min. In realtà per averne un numero sufficiente è necessario > 1h.
- Una piccola quantità di PS può entrare in istmo (ruolo?).

DONNA

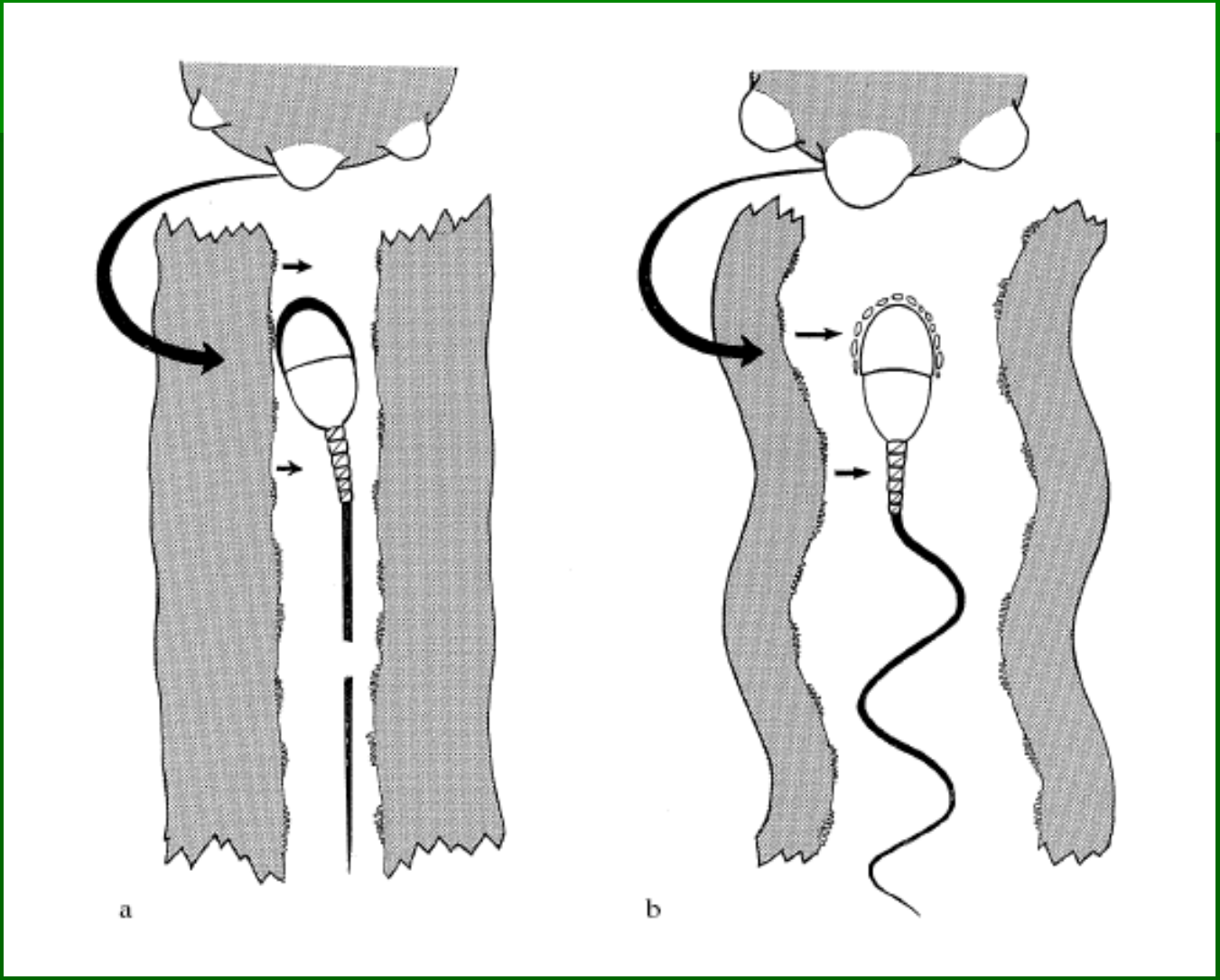


- Scanning electron micrograph showing human sperm attached to a ciliated area of Fallopian tube epithelium *in vitro*. Arrows indicate sperm heads associated with cilia. Scale bar, 4 μm

INTERAZIONI

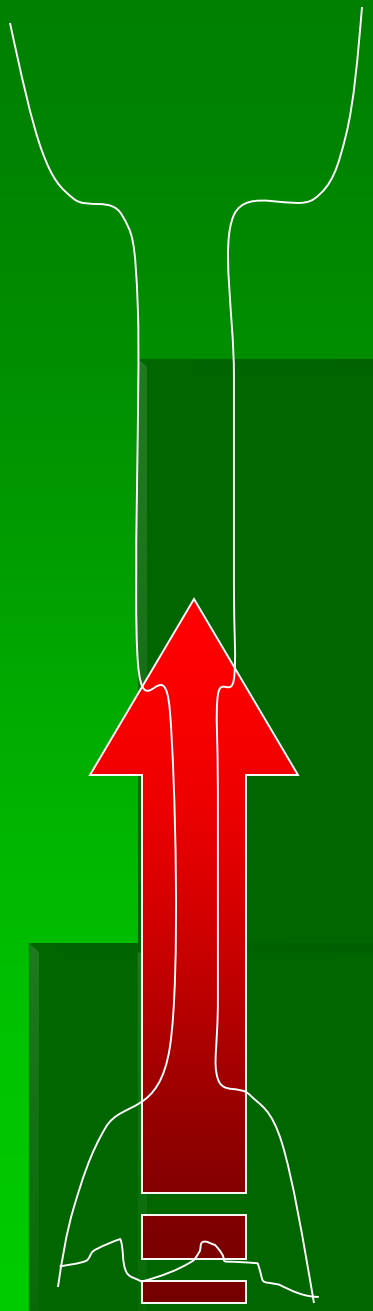


INTERAZIONI



SUINO

Gradiente di concentrazione di spermatozoi



10^2 sptz

10^8 sptz/ml

1. Previene la polispermia
2. Funzione del quadro endocrino

TRASPORTO NELL'ISTMO

- Contrazioni muscolatura liscia pre-/peri-ovulatorie.
- Istmo reservoir funzionale.
- ↑ K^+ e piruvato.
- P4.

INTERAZIONI TUBA-SPERMATOZOO

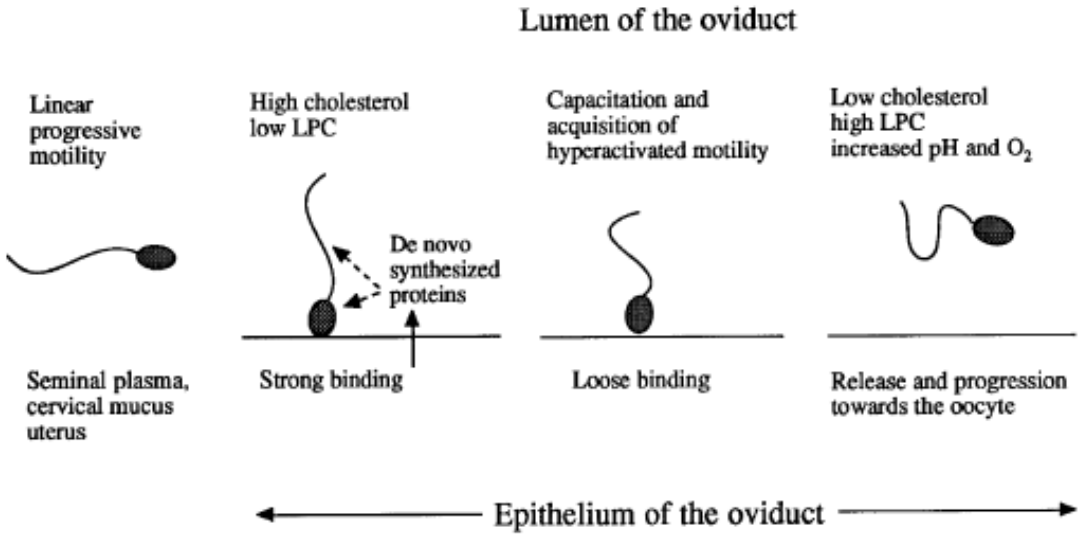
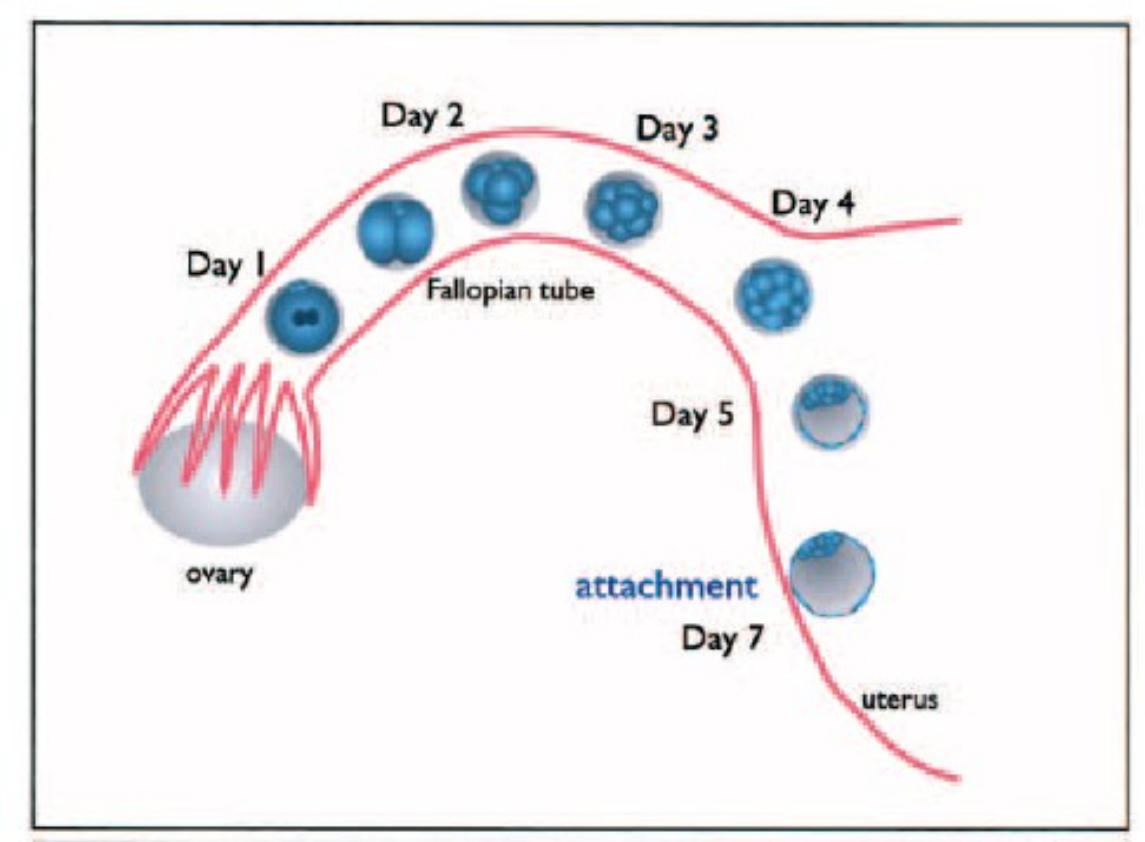


Figure 2. Schematic representation of in-vivo capacitation. Spermatozoa still coated with substances originating from the epididymis and the seminal plasma are not capacitated when they enter the oviduct and their motility is still expected to be linear and progressive. They strongly bind to the epithelial cells (possibly by recognition of sialylated oligosaccharides on the surface of these cells) of the oviduct, which respond by de novo synthesis of a variety of proteins. Specific oviductal proteins bind to spermatozoa and allow maintenance of motility and viability and it is to be expected that they play a role in the regulation of capacitation and its associated membrane changes. During sperm transit in the oviduct, there is a release of sialic acid-recognizing lectins and of decapacitating factors and the hydrolysis of sialic acid from sialoglycoconjugates on the sperm surface. Progesterone is present in the oviductal fluid but its capacitating abilities are probably counterbalanced by the presence of cholesterol or stabilizing proteins, such as oviductin. As ovulation occurs, physical and chemical changes (such as rises in temperature, oxygen, pH, etc.) in the environment may cause the capacitation to resume. The binding of spermatozoa to the epithelium weakens and the acquisition of hyperactivated motility allows spermatozoa to detach from the epithelium and progress further in the oviduct, to regions where the presence of lower concentrations of cholesterol and higher concentrations of lysophosphatidylcholine help in completing the capacitation process.

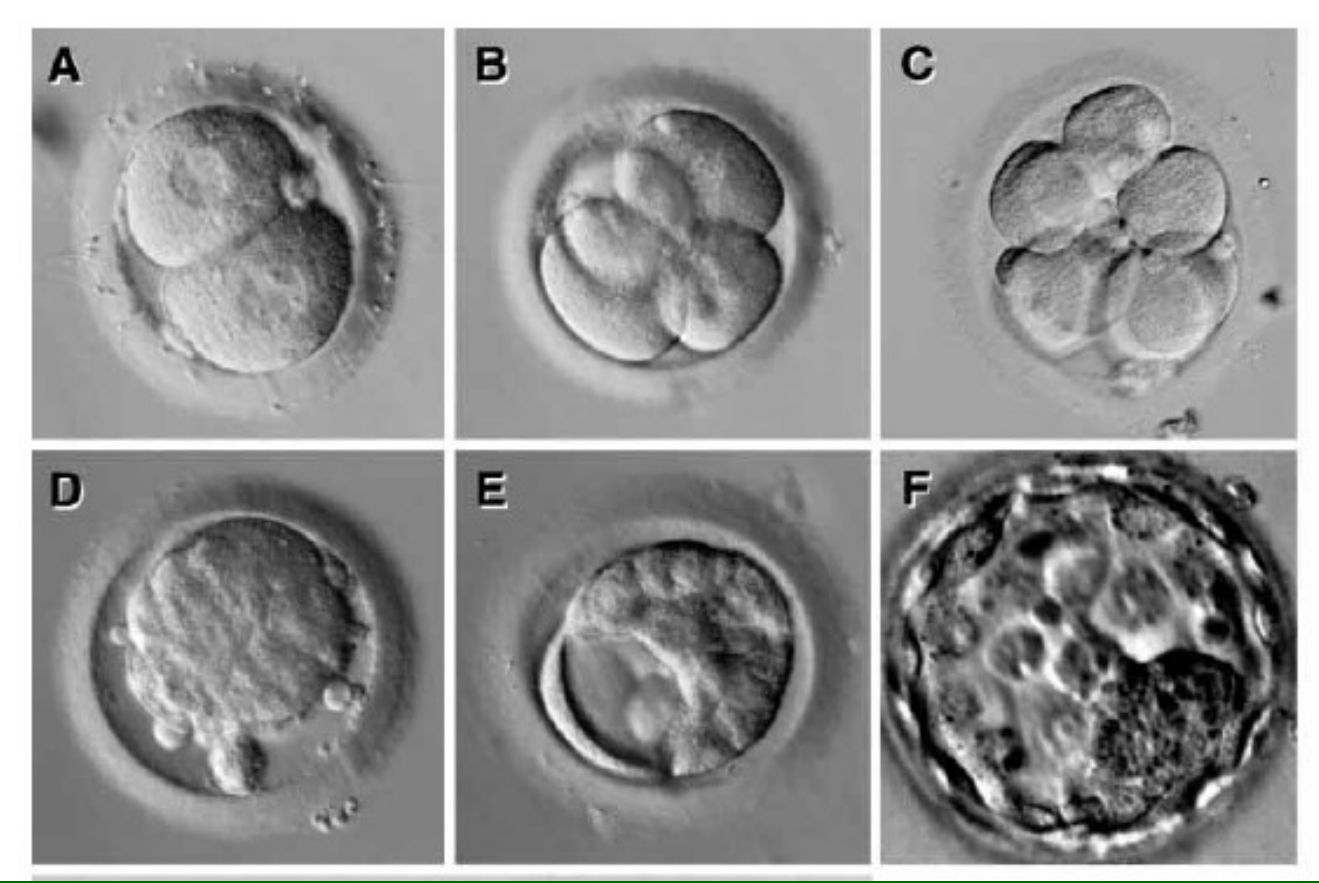
SOPRAVVIVENZA GAMETI

Specie	Oocita (h)	Sptz (h)
Bovino	10 – 12	24 – 48
Ovino	10 – 15	24 – 48
Suino	8 – 12	24 – 42
Equino	8 – 10	140
Uomo	8 – 10	24 – 72

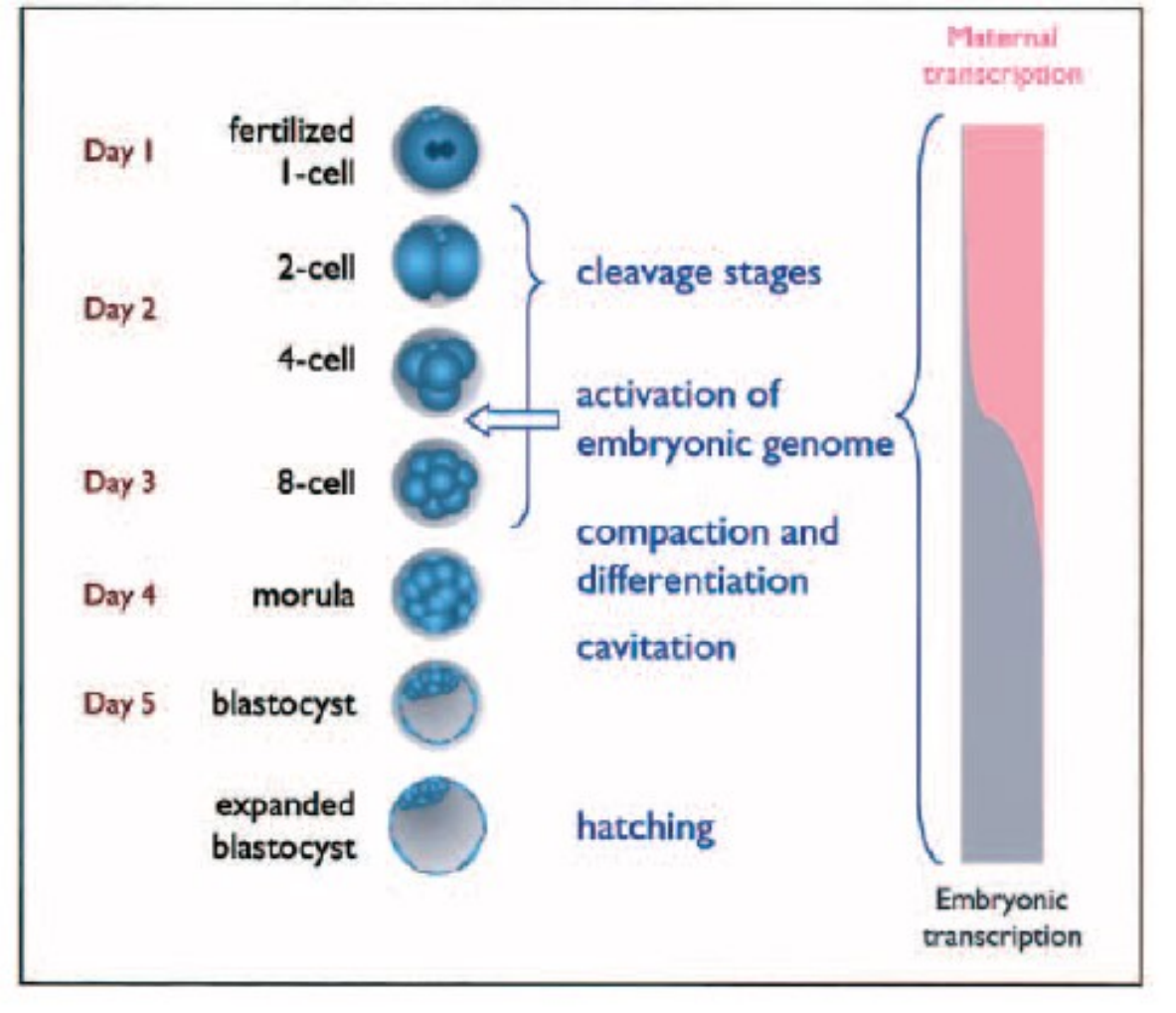
CLEAVAGE


Day 2
Day 3
Day 4
Day 1
Fallopian tube
Day 5
ovary
attachment
Day 7
uterus

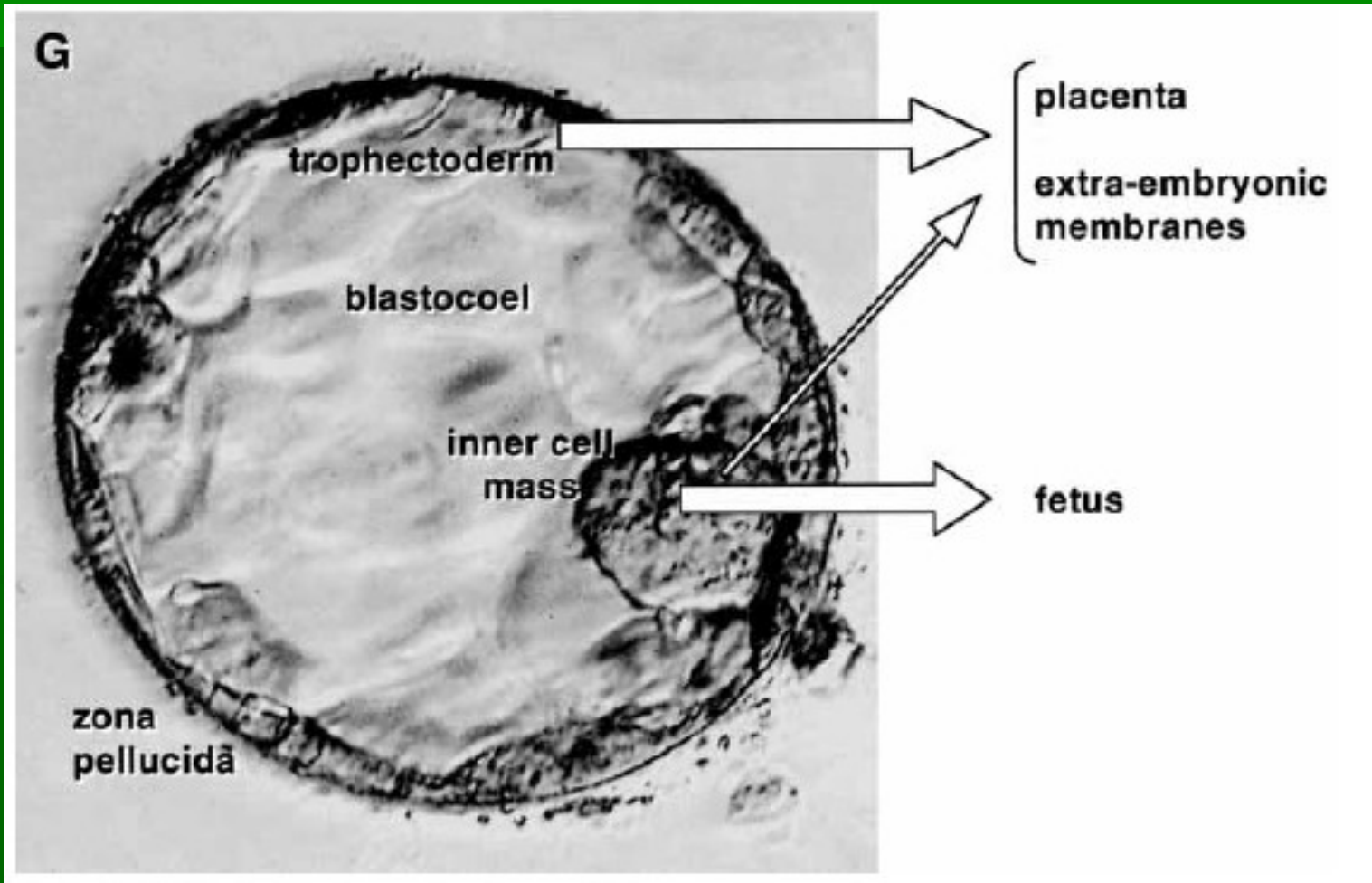
CLEAVAGE

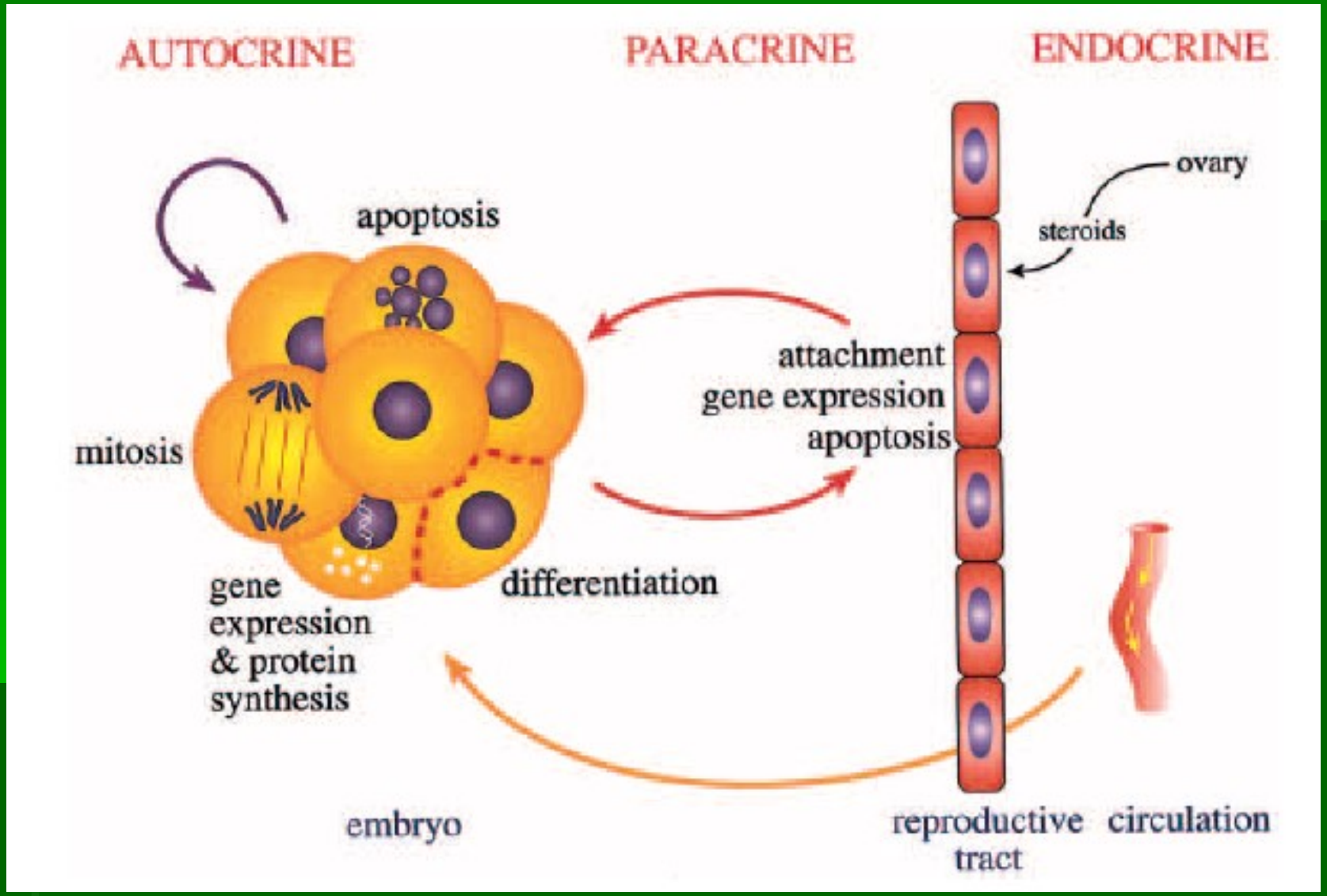


ATTIVAZIONE DELLA TRASCRIZIONE



BLASTOCISTI



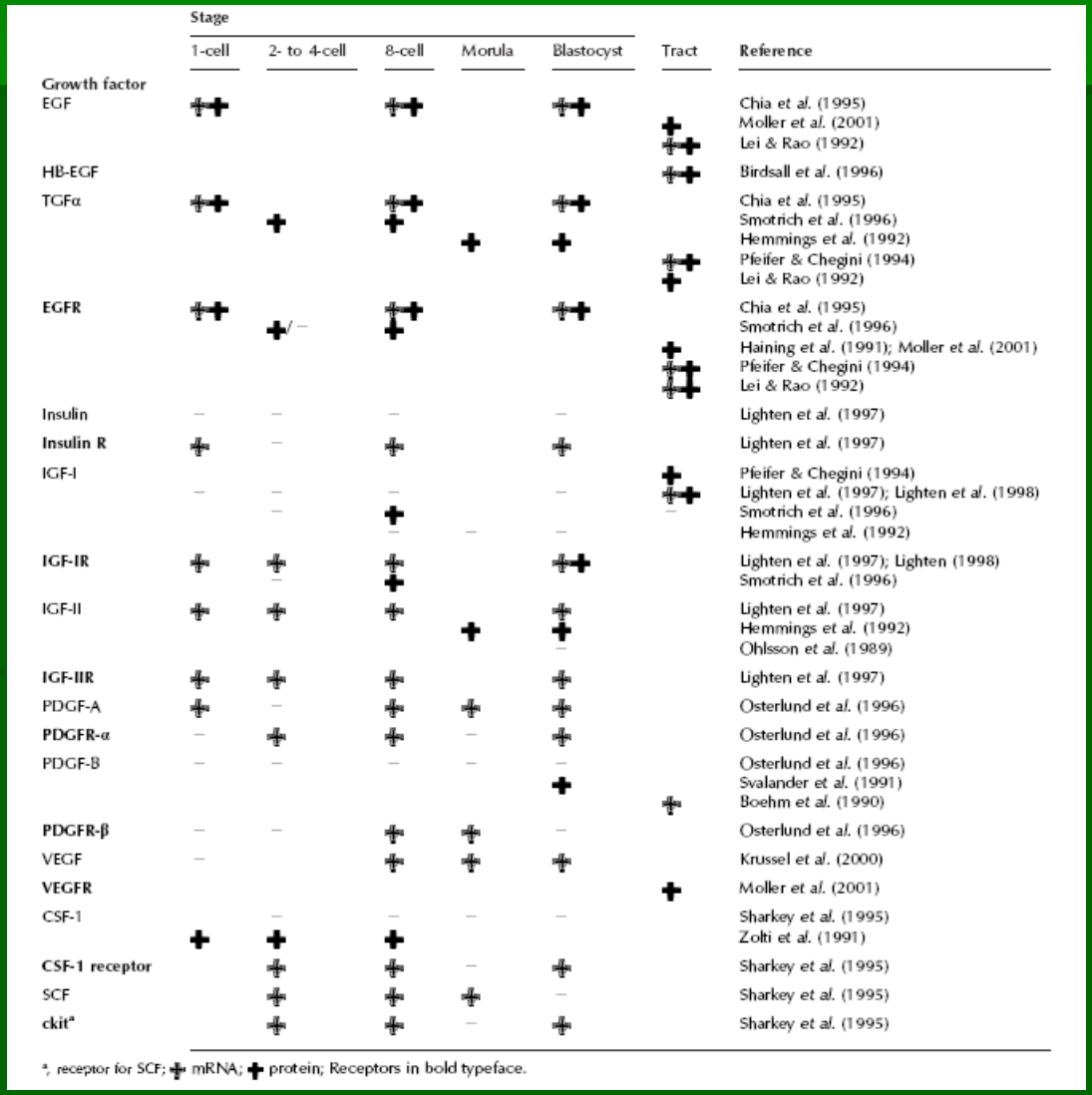

AUTOCRINE
PARACRINE
ENDOCRINE
apoptosis
ovary
steroids
attachment
gene expression
apoptosis
mitosis
differentiation
gene
expression
& protein
synthesis
embryo
reproductive
tract
circulation

FATTORI DI CRESCITA

Table 1 Effects of growth factors and cytokines on mammalian preimplantation development *in vitro*

Effect	Growth factor	Species	Reference
Blastocyst formation ↑	Insulin	Mouse	Harvey & Kaye (1990)
		Cow	Matsui *et al.* (1995)
	IGF-I	Mouse	Harvey & Kaye (1992*a*)
		Cow	Matsui *et al.* (1995); Palma *et al.* (1997)
	IGF-II	Mouse	Harvey & Kaye (1992*b*)
	CSF-1	Mouse	Pampfer *et al.* (1991)
	TGF-α	Cow	Larson *et al.* (1992)
	LIF	Mouse	Lavranos *et al.* (1995)
		Sheep	Fry *et al.* (1992)
	GM-CSF	Cow	de Moraes & Hansen (1997)
		Mouse	Robertson *et al.* (2001)
	HB-EGF	Rat	Tamada *et al.* (1999)
Rate of development ↑	IGF-II	Mouse	Rappolee *et al.* (1992)
	CSF-1	Mouse	Bhatnagar *et al.* (1995)
	PAF	Mouse	Stoddart *et al.* (1996)
	EGF	Mouse	Brice *et al.* (1993)
Blastocyst cell number ↑	IGF-I & -II	Mouse	Rappolee *et al.* (1992)
	GM-CSF	Mouse	Robertson *et al.* (2001)
	PAF	Mouse	Ryan *et al.* (1990*b*)
Specifically ICM ↑	Insulin	Mouse	Harvey & Kaye (1990)
	IGF-I	Mouse	Harvey & Kaye (1992*a*)
	IGF-II	Mouse	Harvey & Kaye (1992*b*)
Specifically TE ↑	CSF-1	Mouse	Bhatnagar *et al.* (1995)
Blastocoel expansion	TGF-α	Mouse	Dardik & Schultz (1991)
	EGF		
Blastocyst hatching/attaching ↑	GM-CSF	Mouse	Robertson *et al.* (2001)
Protein synthesis (TE) ↑	Insulin	Mouse	Harvey & Kaye (1988)
	IGF-II		Rappolee *et al.* (1992)
	EGF		Wood & Kaye (1989)
Protein synthesis (ICM) ↑	TGF-α	Mouse	Dardik *et al.* (1992)
Endocytosis	Insulin	Mouse	Dunglison *et al.* (1995)
Glucose transport	Insulin	Mouse	Kaye *et al.* (1992)
	GM-CSF	Mouse	Robertson *et al.* (2001)
Metabolism	PAF	Mouse	Ryan *et al.* (1990*a*)
Gene expression	IGFs	Mouse	Shi *et al.* (1994)
	TGFs		Babalola & Shultz (1995)
Apoptosis ↓	TGF-α	Mouse	Brison & Schultz (1997)
	PAF	Mouse	O'Neill (1998)
	IGF-I	Rabbit	Herrler *et al.* (1998)
		Mouse	Brison (2000)
Apoptosis ↑	TNF-α	Mouse	Pampfer *et al.* (1997); Wuu *et al.* (1999)

PRODUZIONE FATTORI DI CRESCITA



Growth factor	Stage: 1-cell	2- to 4-cell	8-cell	Morula	Blastocyst	Tract	Reference
EGF	✚✚		✚✚		✚✚	✚	Chia *et al.* (1995)
						✚✚	Moller *et al.* (2001)
							Lei & Rao (1992)
HB-EGF						✚✚	Birdsall *et al.* (1996)
TGFα	✚✚		✚✚		✚✚		Chia *et al.* (1995)
		✚	✚				Smotrich *et al.* (1996)
				✚	✚		Hemmings *et al.* (1992)
						✚✚	Pfeifer & Chegini (1994)
						✚	Lei & Rao (1992)
EGFR	✚✚		✚✚		✚✚		Chia *et al.* (1995)
		✚/–	✚				Smotrich *et al.* (1996)
						✚	Haining *et al.* (1991); Moller *et al.* (2001)
						✚✚	Pfeifer & Chegini (1994)
							Lei & Rao (1992)
Insulin	–	–	–		–		Lighten *et al.* (1997)
Insulin R	✚	–	✚		✚		Lighten *et al.* (1997)
IGF-I						✚	Pfeifer & Chegini (1994)
	–	–	–		–	✚✚	Lighten *et al.* (1997); Lighten *et al.* (1998)
		–	✚			–	Smotrich *et al.* (1996)
			–	–	–		Hemmings *et al.* (1992)
IGF-IR	✚	✚	✚		✚✚		Lighten *et al.* (1997); Lighten (1998)
		–	✚				Smotrich *et al.* (1996)
IGF-II	✚	✚	✚		✚		Lighten *et al.* (1997)
				✚	✚		Hemmings *et al.* (1992)
					–		Ohlsson *et al.* (1989)
IGF-IIR	✚	✚	✚		✚		Lighten *et al.* (1997)
PDGF-A	✚	–	✚	✚	✚		Osterlund *et al.* (1996)
PDGFR-α	–	✚	✚	–	✚		Osterlund *et al.* (1996)
PDGF-B	–	–	–	–	–		Osterlund *et al.* (1996)
					✚		Svalander *et al.* (1991)
						✚	Boehm *et al.* (1990)
PDGFR-β	–	–	✚	✚	–		Osterlund *et al.* (1996)
VEGF	–		✚	✚	✚		Krussel *et al.* (2000)
VEGFR						✚	Moller *et al.* (2001)
CSF-1		–	–	–	–		Sharkey *et al.* (1995)
	✚	✚	✚				Zolti *et al.* (1991)
CSF-1 receptor		✚	✚	–	✚		Sharkey *et al.* (1995)
SCF		✚	✚	✚	–		Sharkey *et al.* (1995)
ckit[a]		✚	✚	–	✚		Sharkey *et al.* (1995)

[a], receptor for SCF; ✚ mRNA; ✚ protein; Receptors in bold typeface.

PRODUZIONE FATTORI DI CRESCITA

Growth factor	Stage: 1-cell	2- to 4-cell	8-cell	Morula	Blastocyst	Tract	Reference
VEGF	–		✙	✙	✙		Krussel *et al.* (2000)
VEGFR						✚	Moller *et al.* (2001)
LIF	–	–	–	–	–		Sharkey *et al.* (1995)
	✙	✙	✙	✙	✙		Chen *et al.* (1999)
						✙	Charnock-Jones *et al.* (1994)
						✙✚	Cullinan *et al.* (1996)
LIF-R					✙		Charnock-Jones *et al.* (1994)
	–	–	–	–	✙		Sharkey *et al.* (1995)
	✙	✙	✙	✙	✙		Chen *et al.* (1999)
	✙	✙	✙		✙		van Eijk *et al.* (1996)
						✙✚	Cullinan *et al.* (1996)
TNF-α		–	✙	–	–		Sharkey *et al.* (1995)
			✚				Zolti *et al.* (1991)
TNF-R		✙	✙	–	–		Sharkey *et al.* (1995)
GM-CSF						✚	Giacomini *et al.* (1995)
						✙✚	Zhao & Chegini (1999)
PAF		✚					Collier *et al.* (1990)
PAF-R		–	–	–	–		Sharkey *et al.* (1995)
						✙✚	Ahmed *et al.* (1998)
IL-1	✚	✚	✚				Zolti *et al.* (1991)
IL-1β	✚	✚	✚	✚	✚		De los Santo *et al.* (1996)
IL-1R t1	✚	✚	✚	–	✚		De los Santos *et al.* (1996)
						✙	Simon *et al.* (1993)
IL-6		–	–	–	✙		Sharkey *et al.* (1995)
	✚	✚	✚				Zolti *et al.* (1991)
IL-6-R		–	–	–	✙		Sharkey *et al.* (1995)
TGFβR-T1	✙✚	–	–		✙		Osterlund & Fried (2000)
TGFβ-T2	✙✚	–	–		–		Osterlund & Fried (2000)

✙ mRNA; ✚ protein; Receptors in bold typeface; IL-1R t1, interleukin-1 receptor type 1; TGFβR-T1, TGFβ receptor type 1; TGFβR-T2, TGFβ receptor type 2.

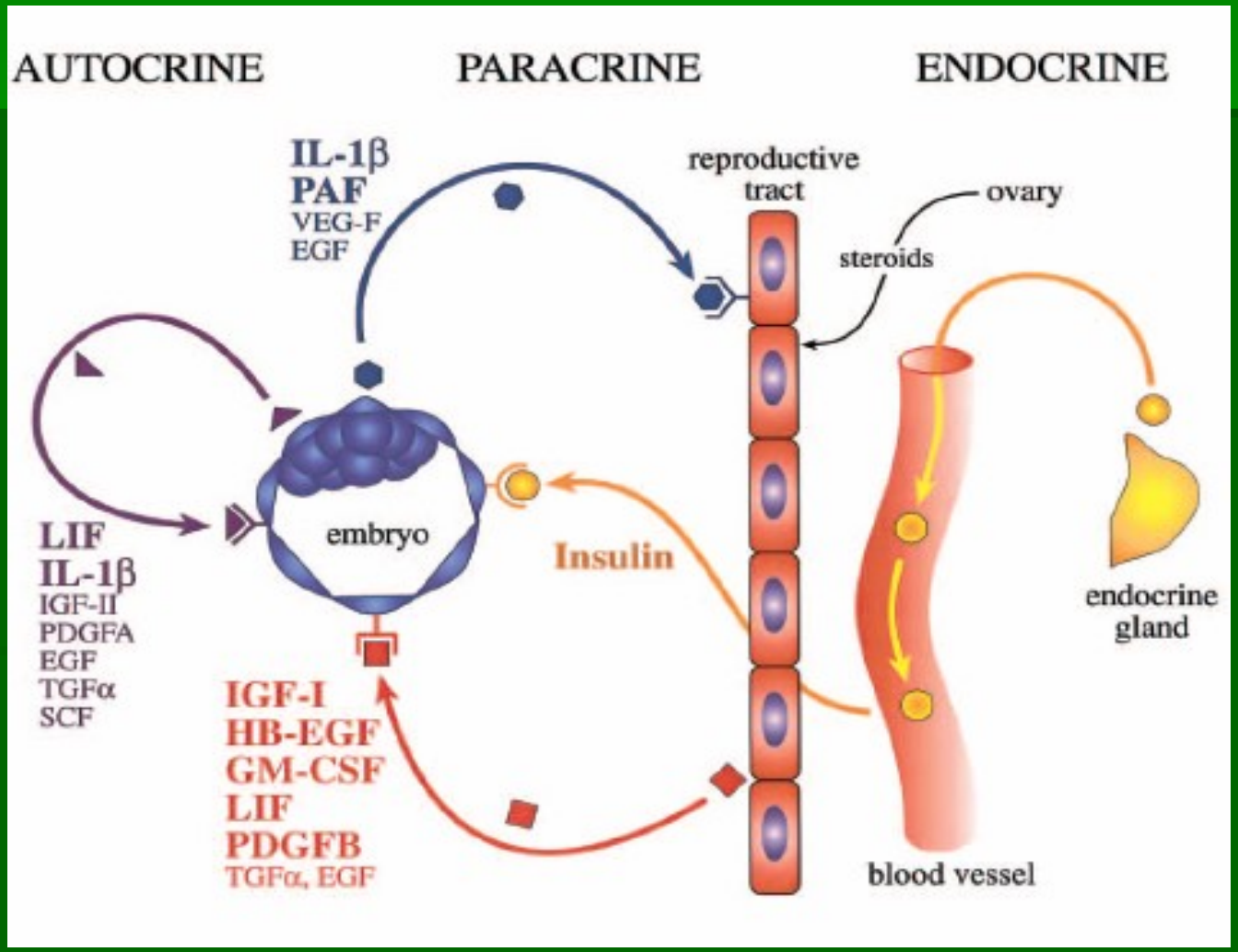
EFFETTO *IN VITRO*

Table 4 Effects of growth factors on preimplantation human development *in vitro*

	Concentration studied	% of embryos forming blastocysts	Blastocyst cell number	Metabolism	Other effects
Growth-factor					
PAF[1]	0·2–1·5 μM	na	na	↑ CO_2 production from glucose	↑ Pregnancy rate following IVF/ET
LIF[2]	5–20 ng/ml	no change	na	na	
LIF[3]	1000 i.u./ml	↑ (18 to 44%)	na	na	↑ Hatching
Insulin[4]	100 ng/ml	No change (46–66%)	No change	↑ Lactate production	↑ Protein synthesis
Insulin[5]	25 μg/ml	Not applicable	Not applicable	Not applicable	↑ hCG production by day 7 blastocysts
PDGF[5]	2 ng/ml	Not applicable	Not applicable	Not applicable	↑ hCG production by day 7 blastocysts
HB-EGF[6]	1–100 nM	↑ (41 to 71%)	No change	No change	↑ hCG production
IGF-I[7,8]	1·7 nM	↑ (35 to 60%)	↑ ICM by 60%	No change	
IGF-I[9]	1·7 nM	↑ (49 to 74%)	No change (total) ICM na	na	↓ Apoptosis by 50%
GM-CSF[10]	2 ng/ml	↑ (30 to 76%)	↑ ICM by 35%	na	↑ Rate of development ↑ Attachment and TE outgrowth

na, not analysed; [1]O'Neill *et al.* (1989); [2]Jurisicova *et al.* (1995); [3]Dunglison *et al.* (1996); [4]Conaghan (1996); [5]Lopata & Oliva (1993); [6]Martin *et al.* (1998); [7]Lighten *et al.* (1998); [8]Lighten (1998); [9]Spanos *et al.* (2000); [10]Sjoblom *et al.* (1999).

MODELLO


AUTOCRINE
PARACRINE
ENDOCRINE
IL-1β
PAF
VEG-F
EGF
reproductive tract
ovary
steroids
LIF
IL-1β
IGF-II
PDGFA
EGF
TGFα
SCF
embryo
Insulin
endocrine gland
IGF-I
HB-EGF
GM-CSF
LIF
PDGFB
TGFα, EGF
blood vessel