

RECENT RESEARCH IN
CERVICAL SECRETION: SOME
BIOPHYSICAL ASPECTS
(Odeblad, E., Menárguez, M.)



Cervical secretion

Cervical secretion

- Cervical mucus is an hydrogel produced by the cérvix glands.
- It is involved in sperm migration and maturation through the female genital tract, and provides a barrier to prevent the pathogens entering the endometrium.

Cervical secretion

- This mucus changes with the menstrual cycle, which means it has different biophysical and biochemical characteristics throughout the cycle.
- Mucus is therefore an indirect but important element for identifying ovulation, not only for clinicians but also for women using natural family planning methods.

Cervical secretion

- Nowadays, we know that cervical mucus is not a homogeneous entity.
- It would therefore be a heterogeneous entity, containing different types of secretion, which percentages that vary throughout the cycle.

Cervical secretion

- The previous studies by Odeblad, indicate that human cervical mucus, contains four different types of secretion, called G (gestagenic), L (loaf), S (string) and P (peak) mucus, with different viscosities (NMR) and a different morphology in the crystals of air-dried mucus samples.

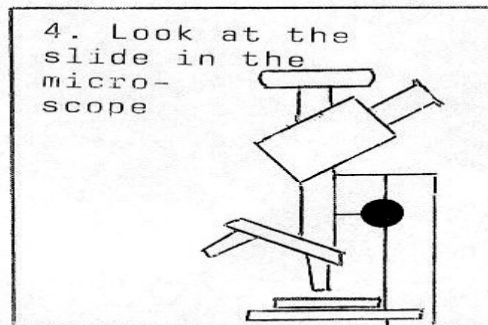
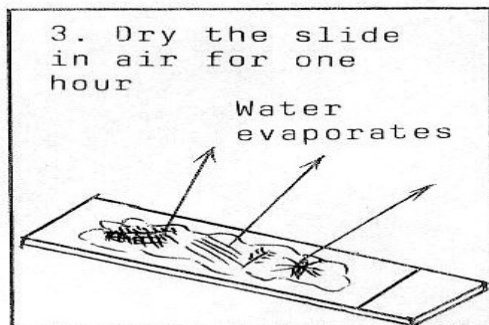
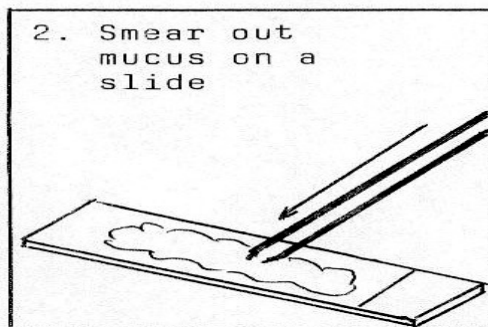
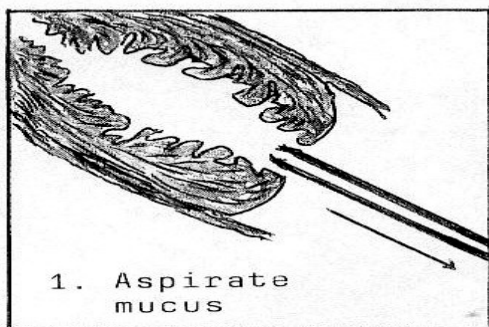


Fig. 3.

Four different mucus types

- Estrogenic mucus types: L, S and P.
- Gestagenic mucus type: G.

L MUCUS

L MUCUS: estrogenic; 6-7 days before ovulation

- L mucus: it had the typical “ferning” morphology. We observed that it had a structure with a straight or curved axis and branches protruding from it at 90° angle. These branches could also act as an axis for new branches, again at a 90° angle.

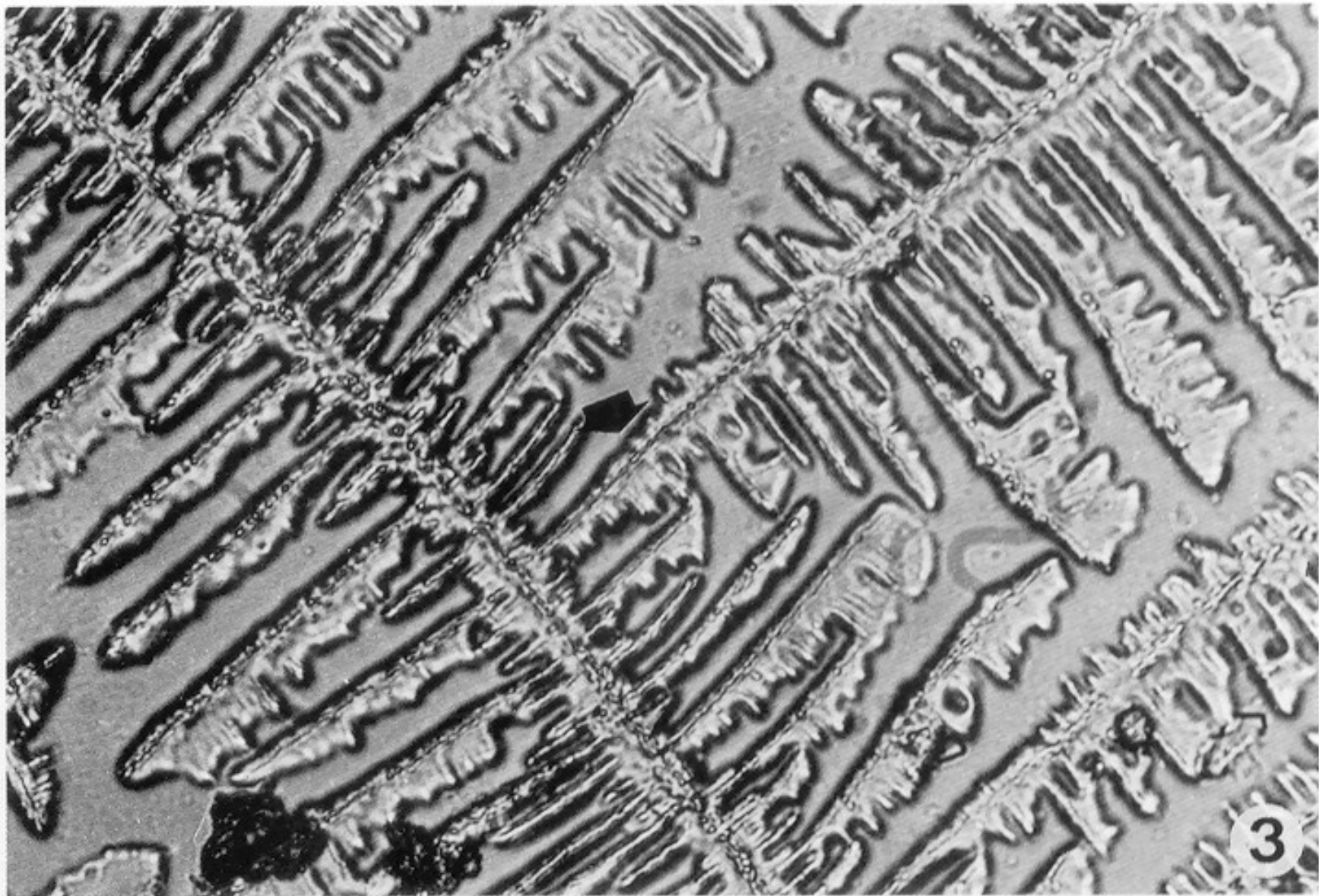
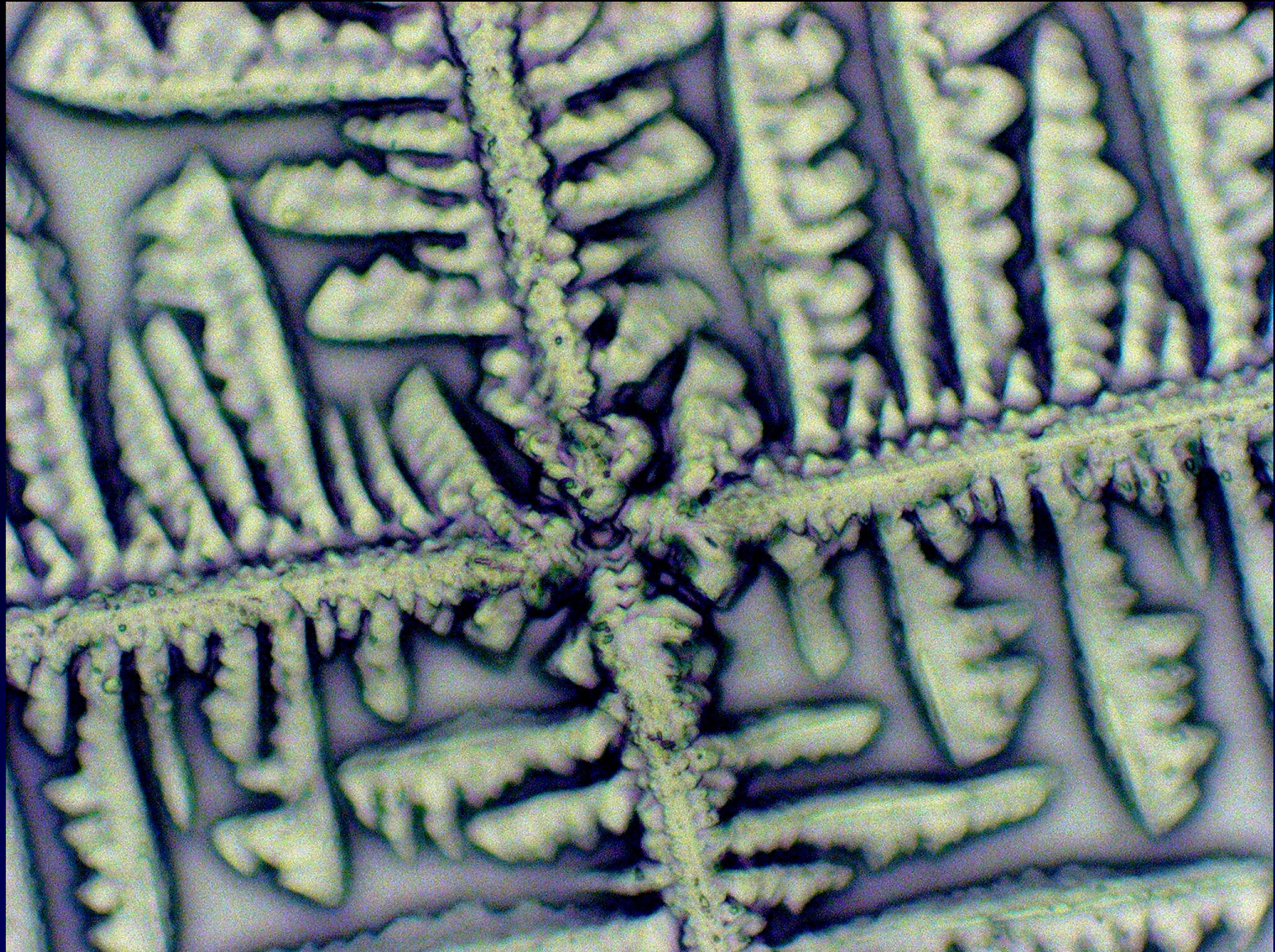
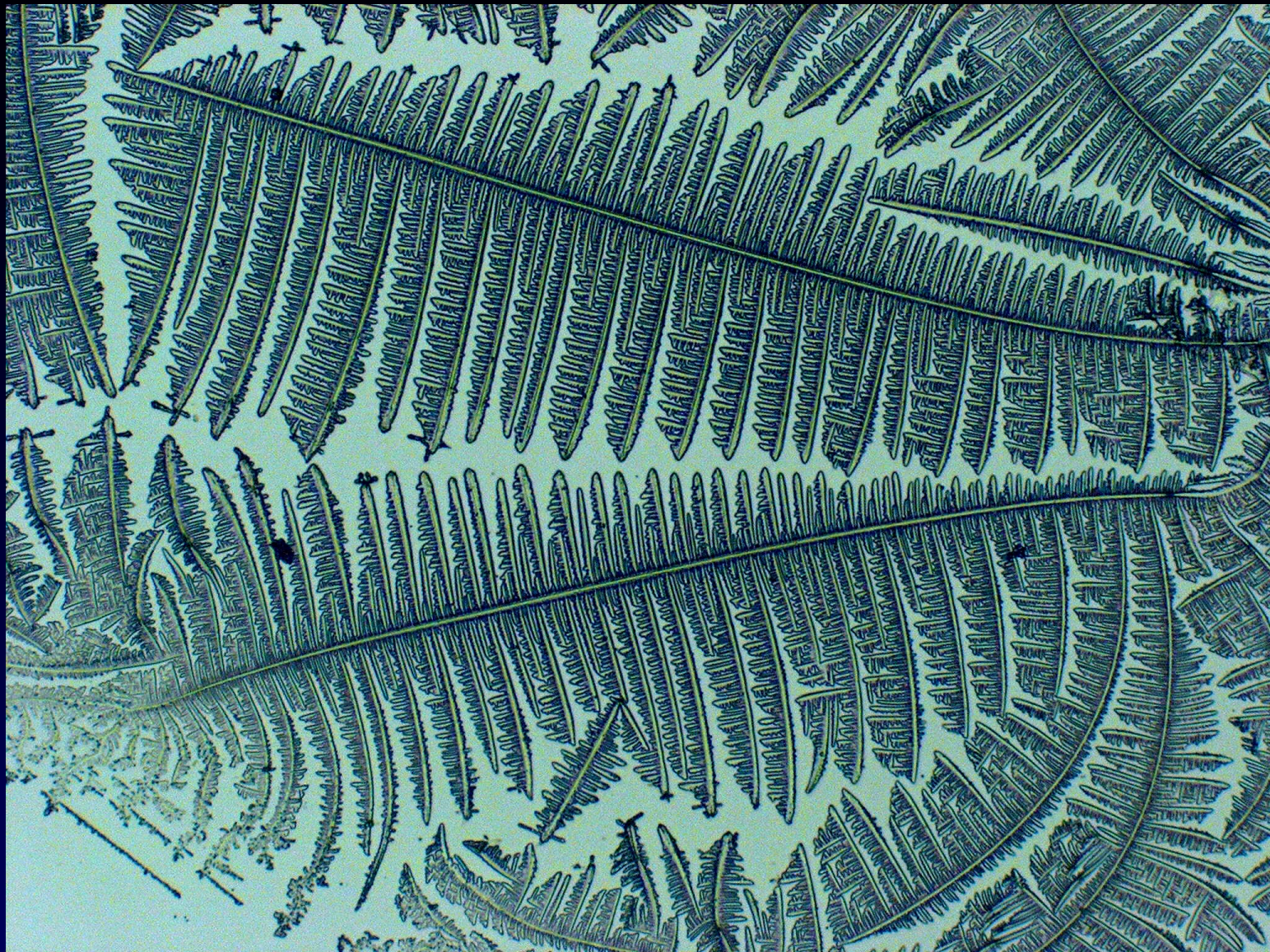
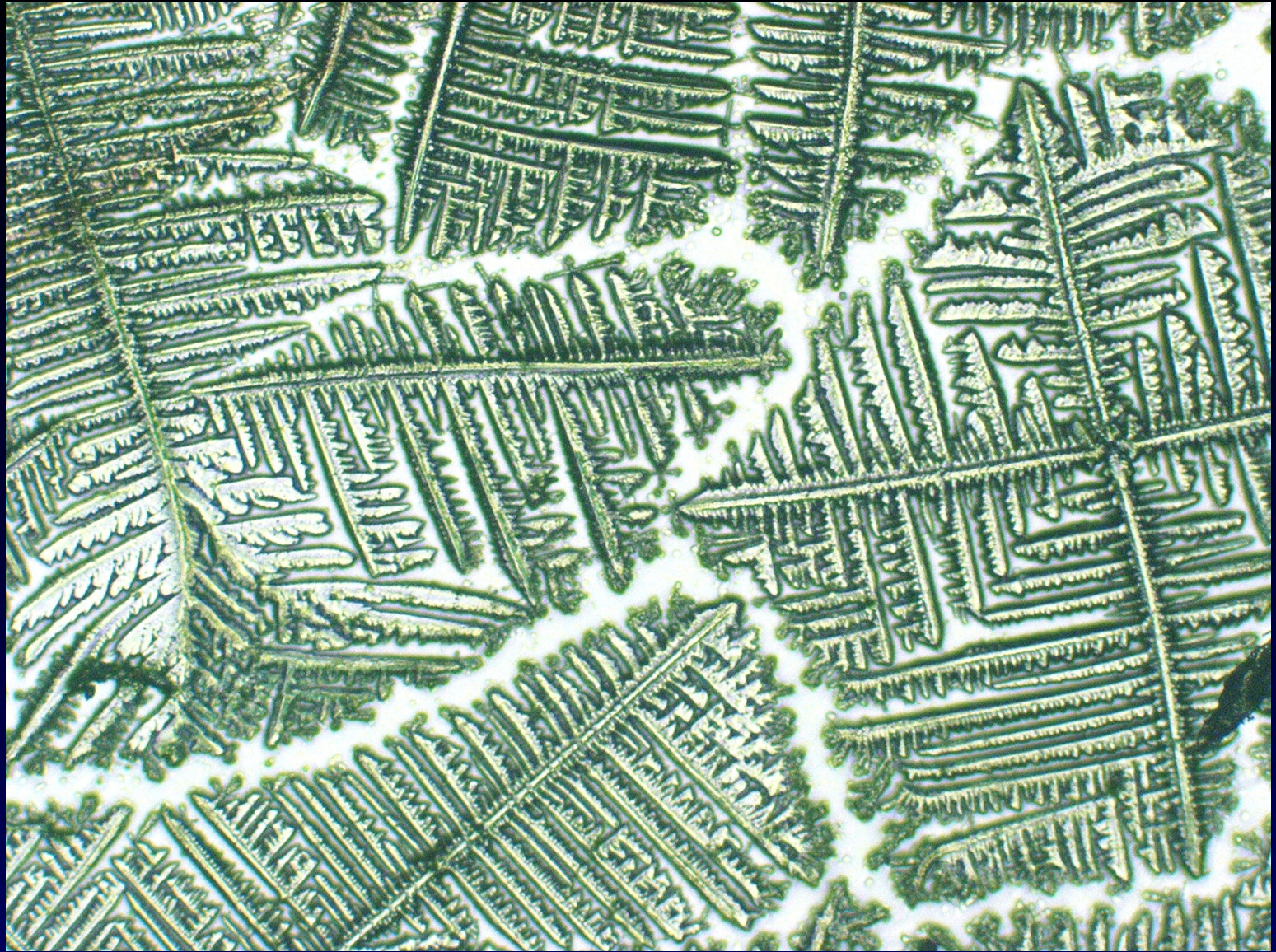


Fig. 3. En el interior del eje principal se identifican pequeños cristales. Se observa cómo de los ejes principales nacen otros secundarios (flecha corta). Muestra 17S. ML x 40.

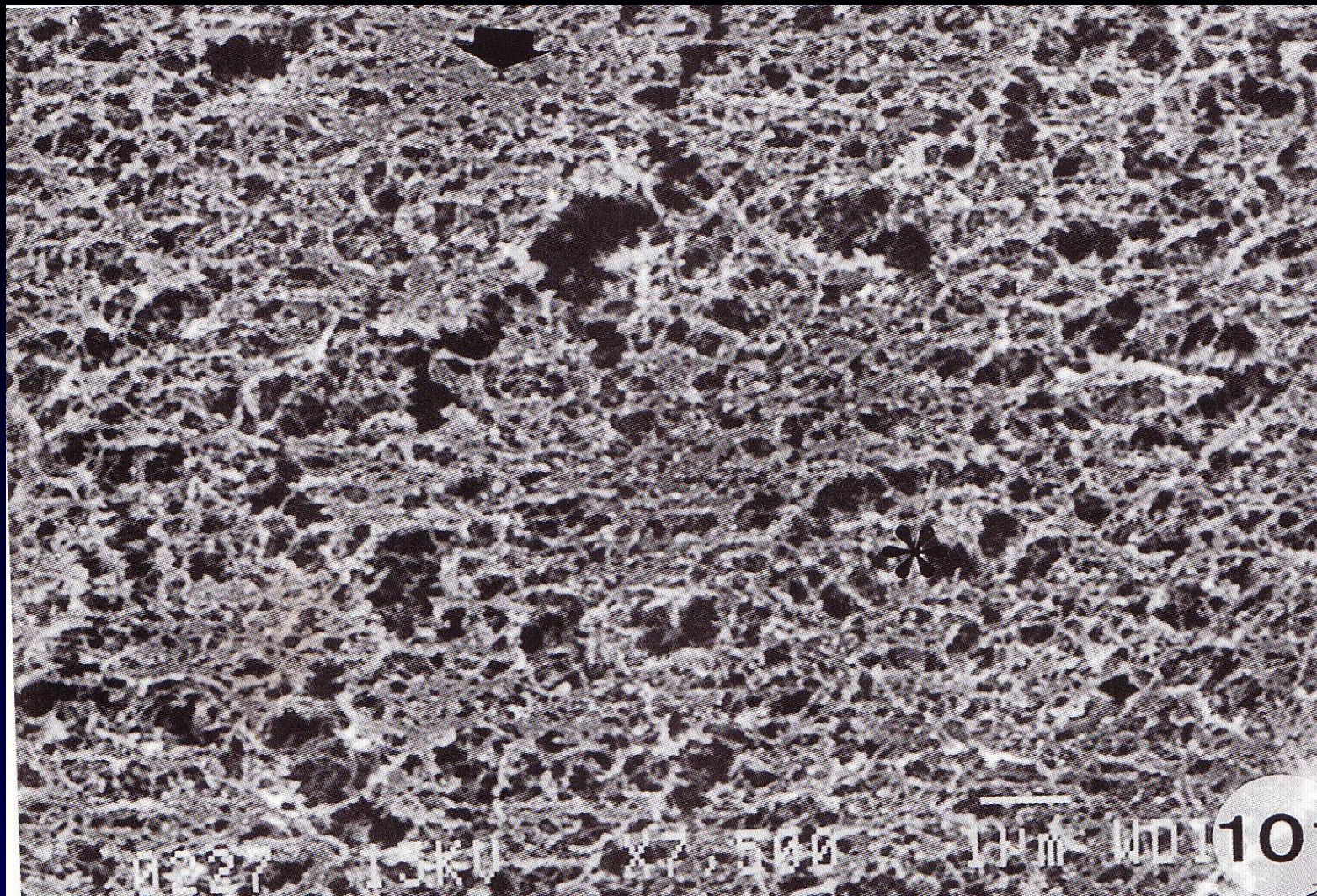






L MUCUS

- In the fixed samples from the cervical canal, a structure similar to a marine sponge was founded in the samples with a high percentage of L mucus. The pores had diameters of 0.4-1.3 μm .



M227

1.5kV

X7,500

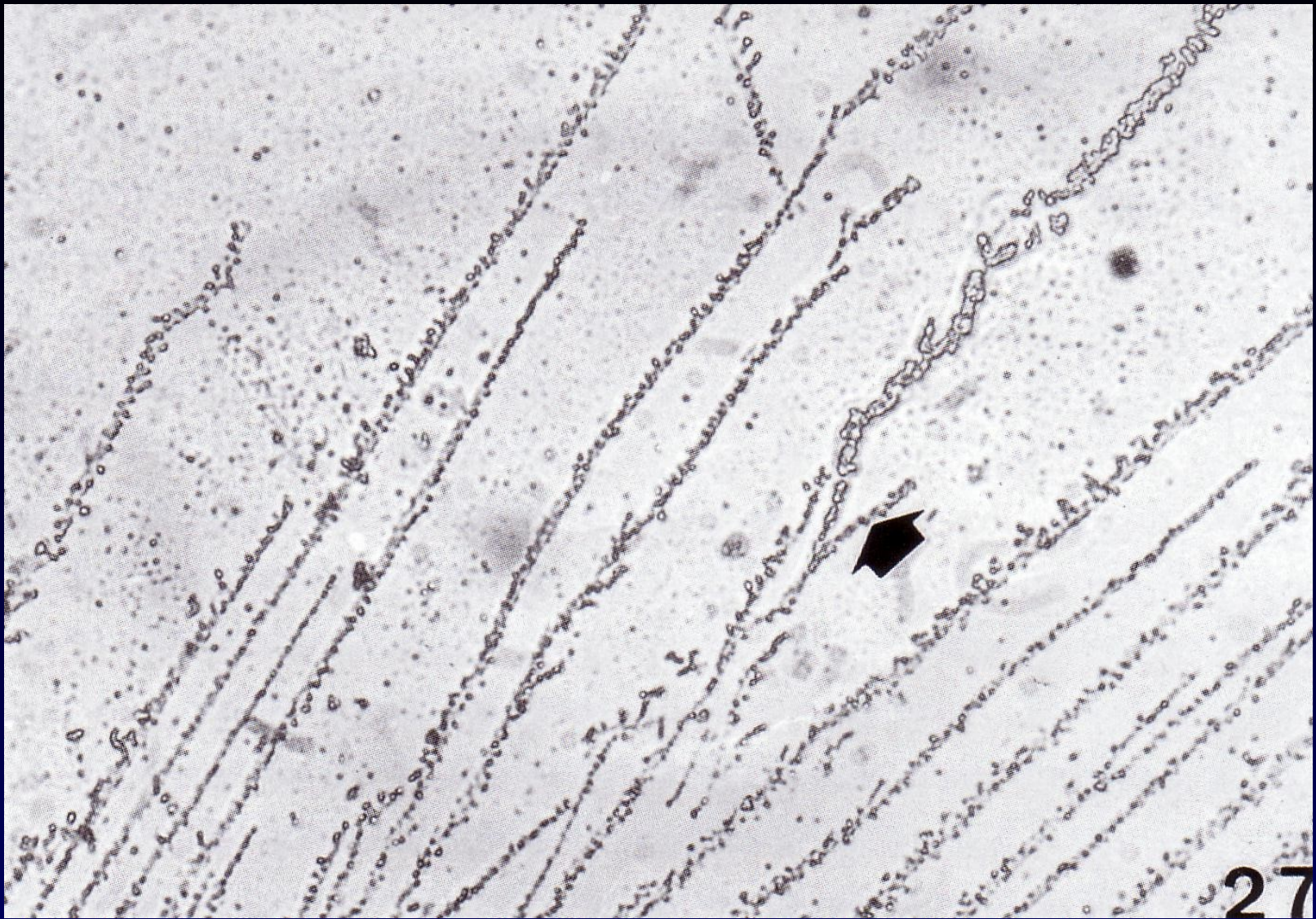
10 μm

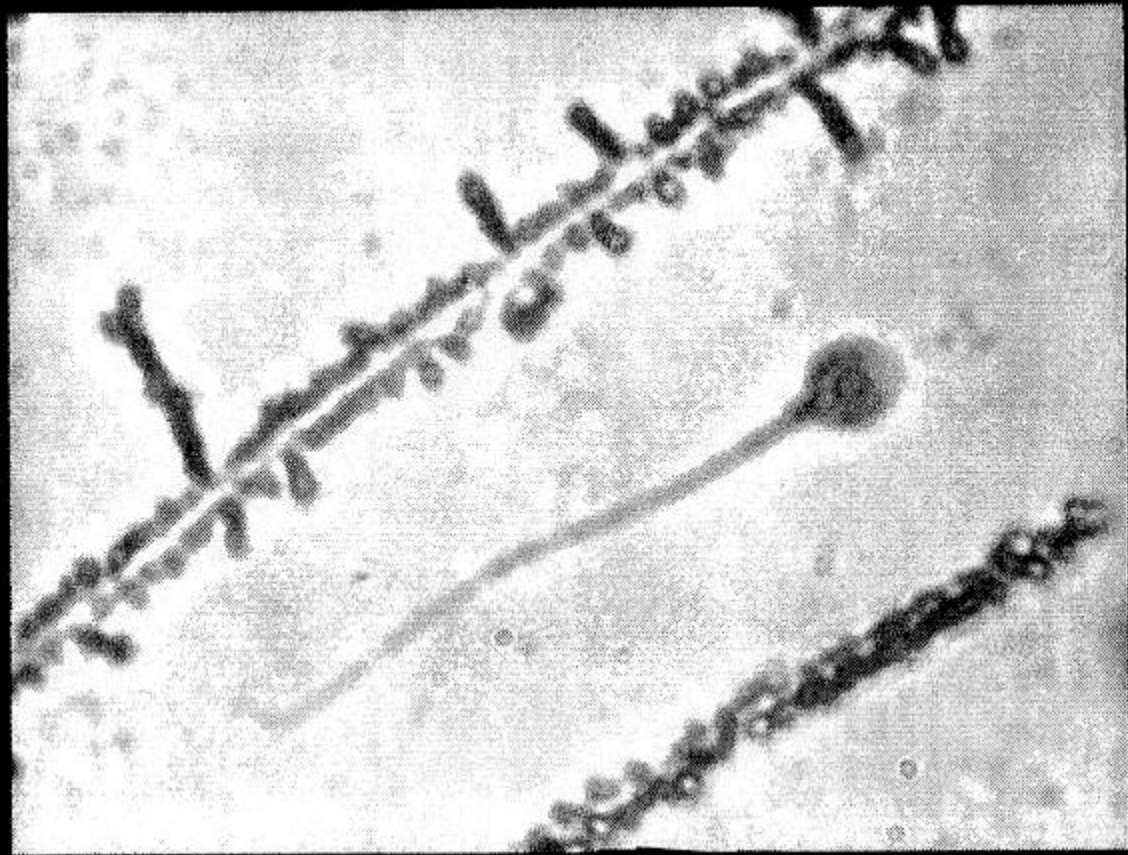
WD 110

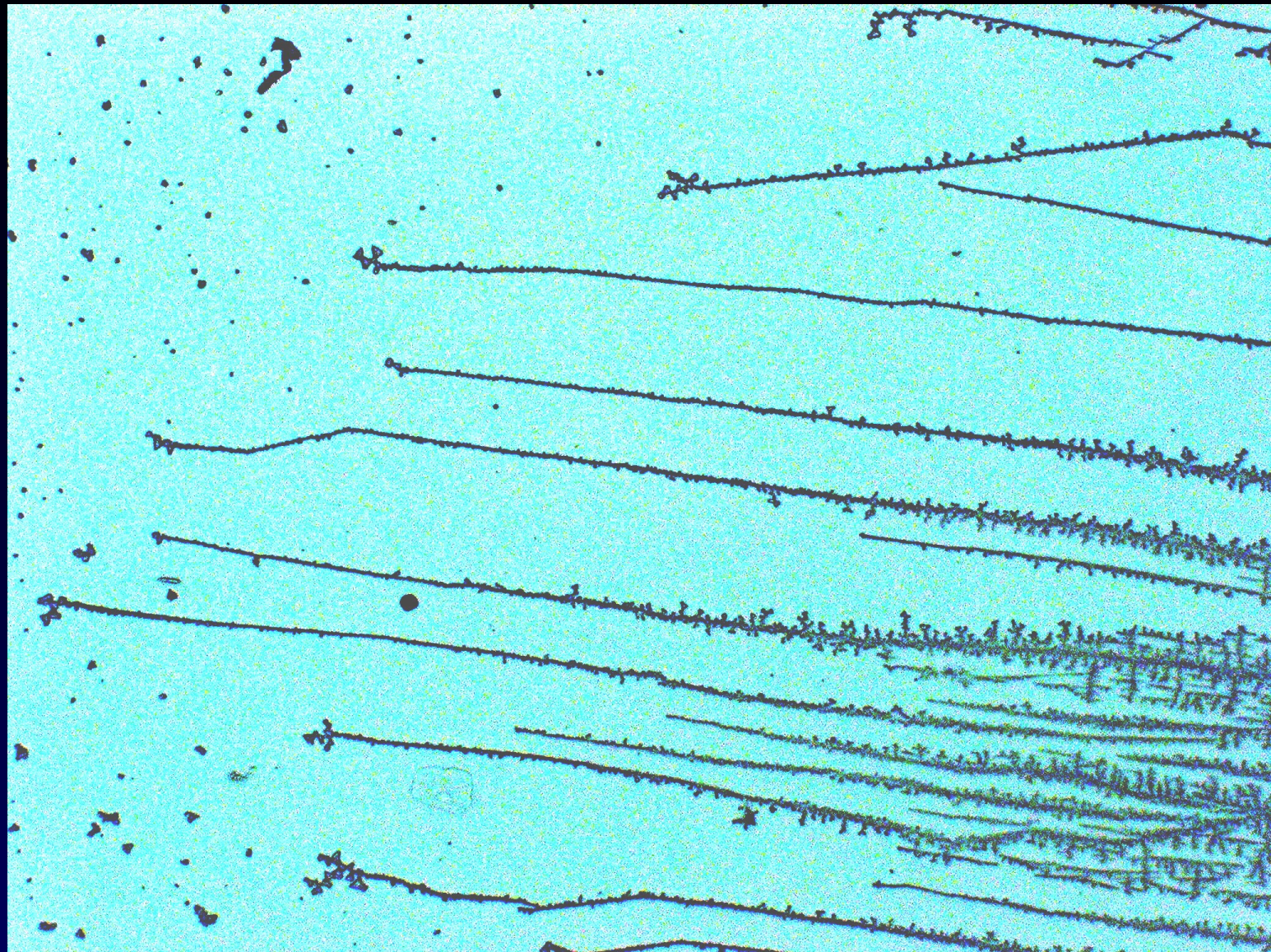
S MUCUS

S MUCUS: estrogenic, 2-3 days before ovulation

- In the air dried samples, S mucus consists of a parallel arrangement of crystals, sometimes with little branches.







0101

15KV

X650

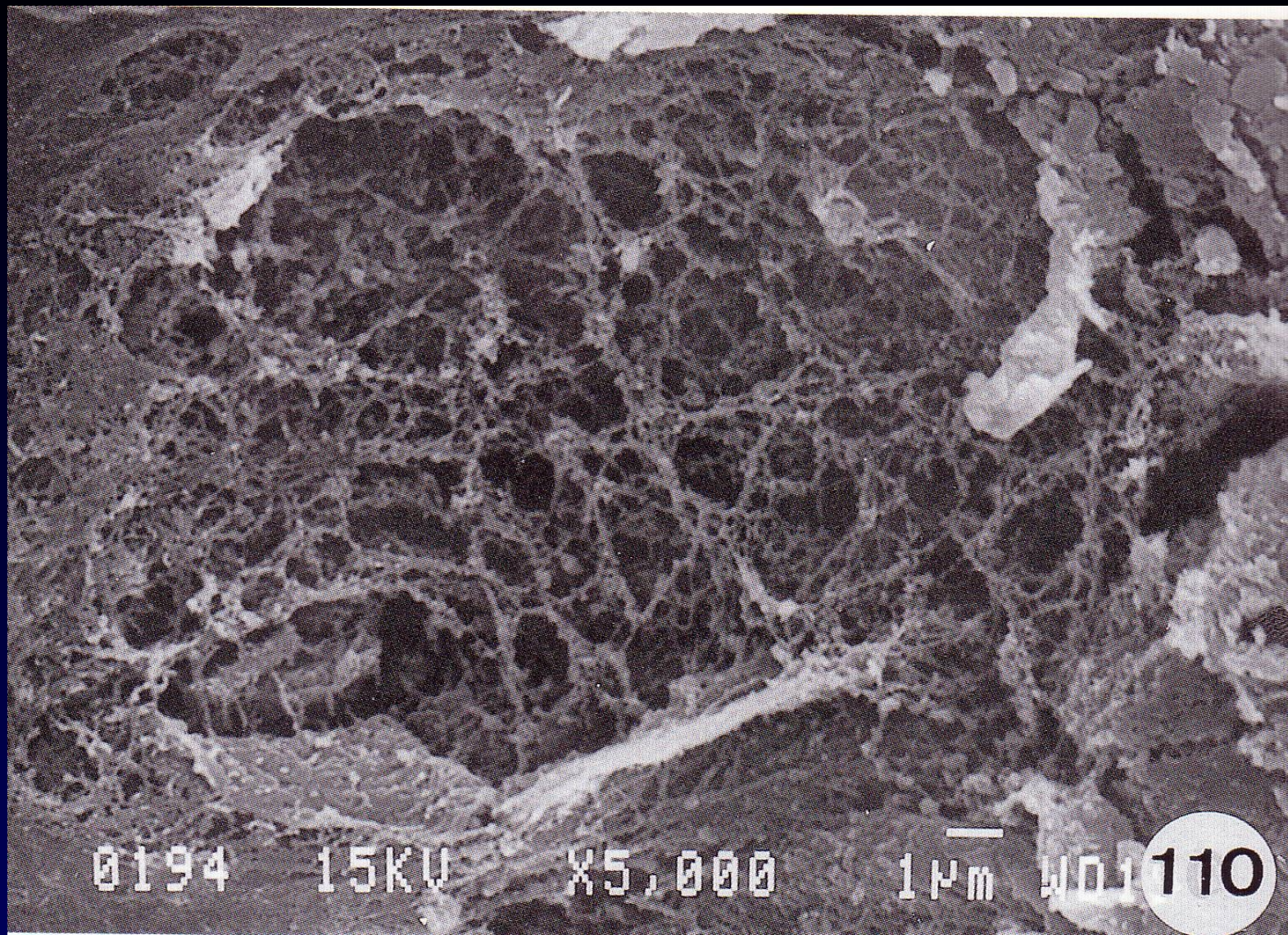
10µm

WD16

39

S MUCUS

- In the fixed mucus samples, S mucus presents a networking of parallel or crossing fibres, with pores of a greater diameter (1.5-7 μ m) than the L ones.



0194

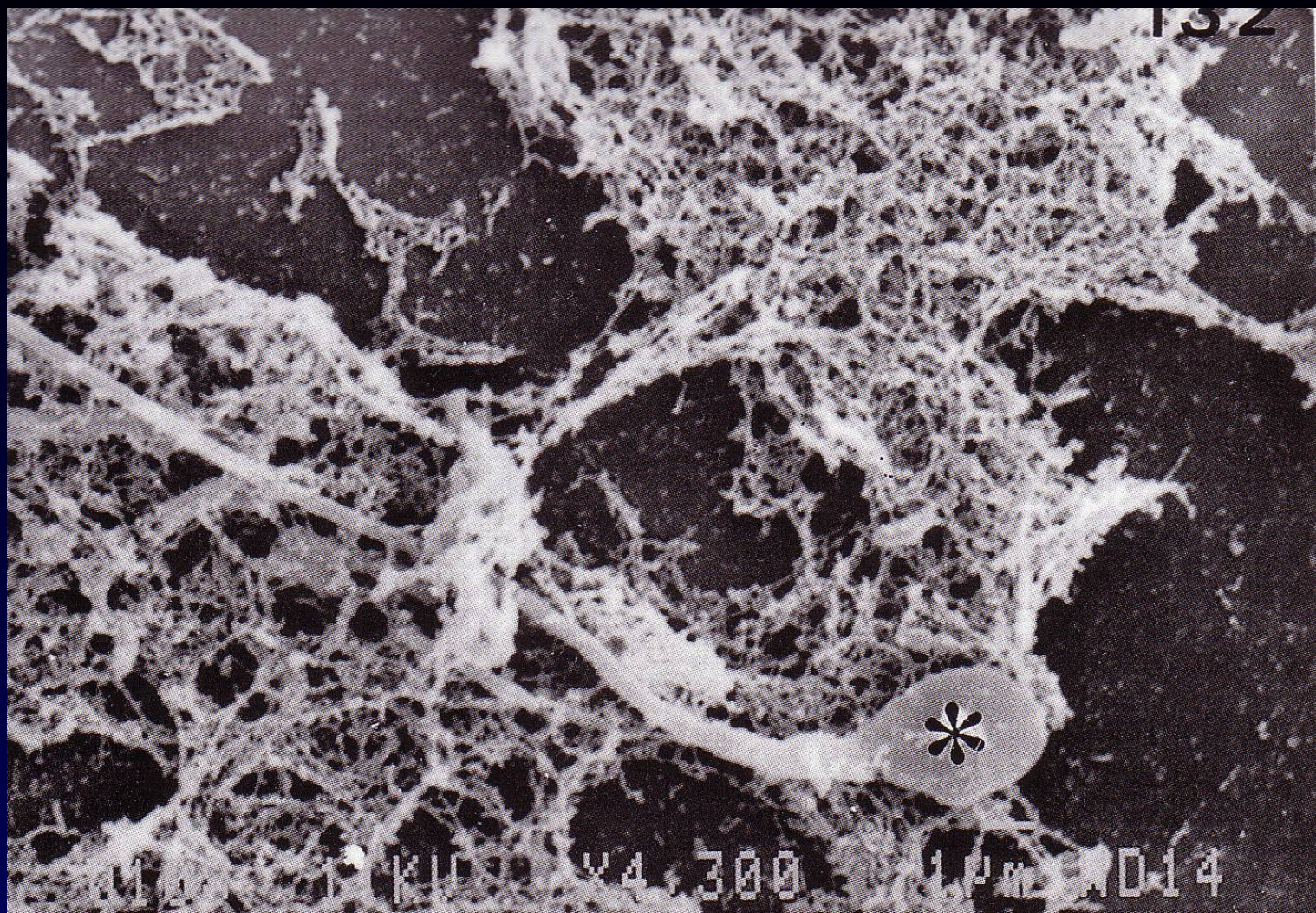
15KV

X5,000

1µm

WD1

110



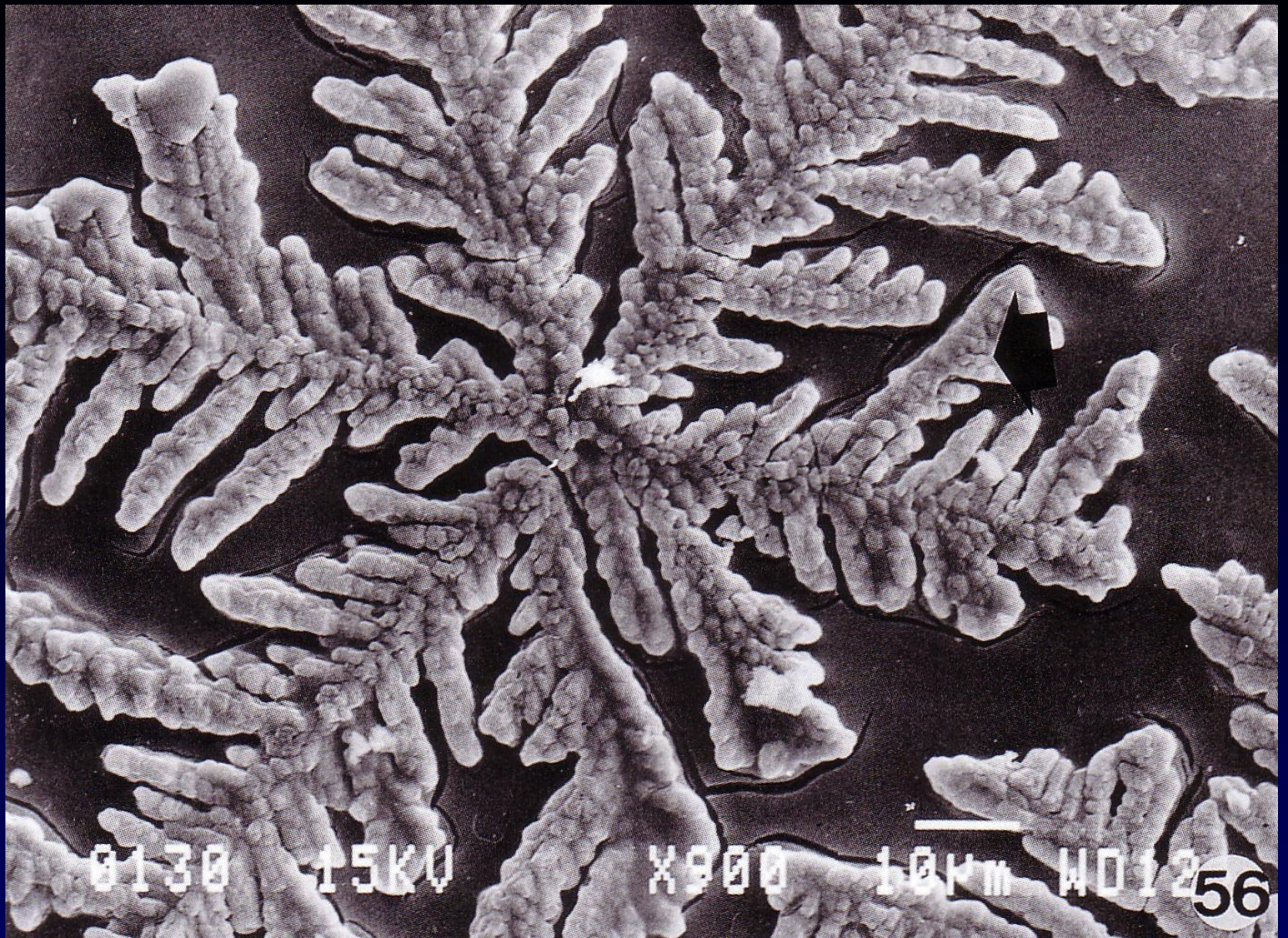
132

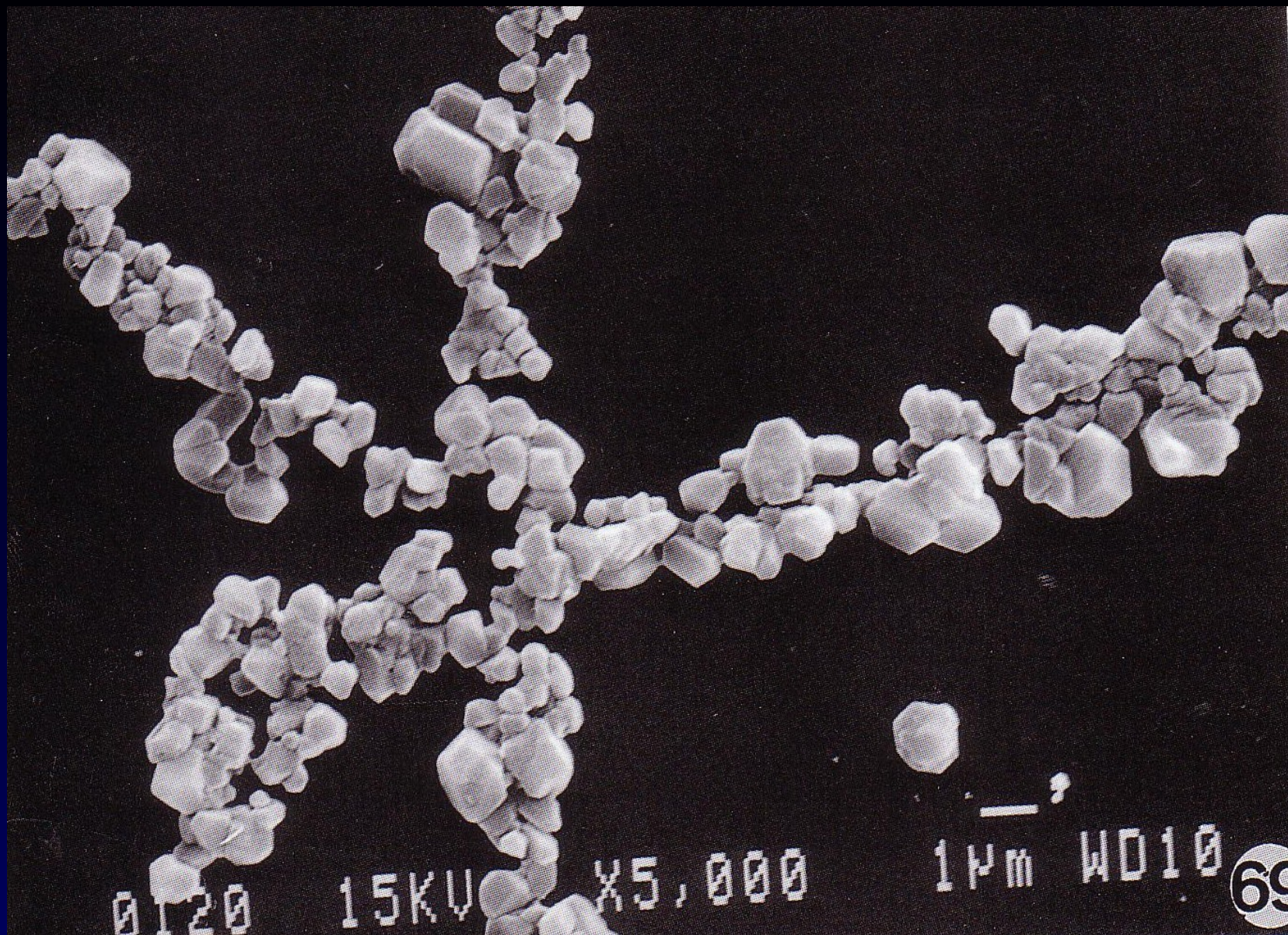
1000 X 4.300 1.0um MD14

P MUCUS

P mucus: estrogenic; peak day

- P mucus: we found five different subtypes;
- P6B: presented a star-like morphology with six well-defined axes. There were branches protruding from the axes at a 60° angle.



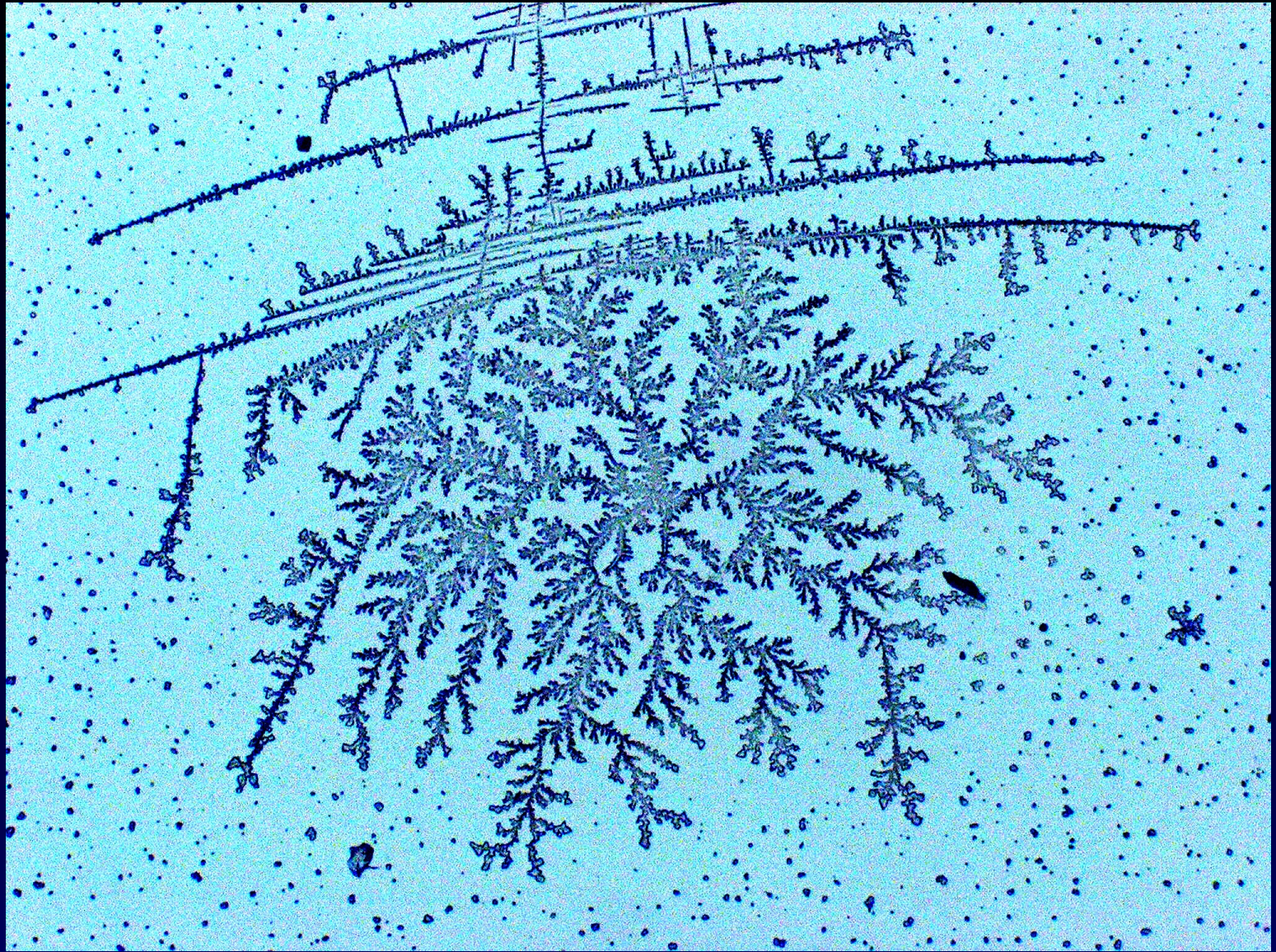


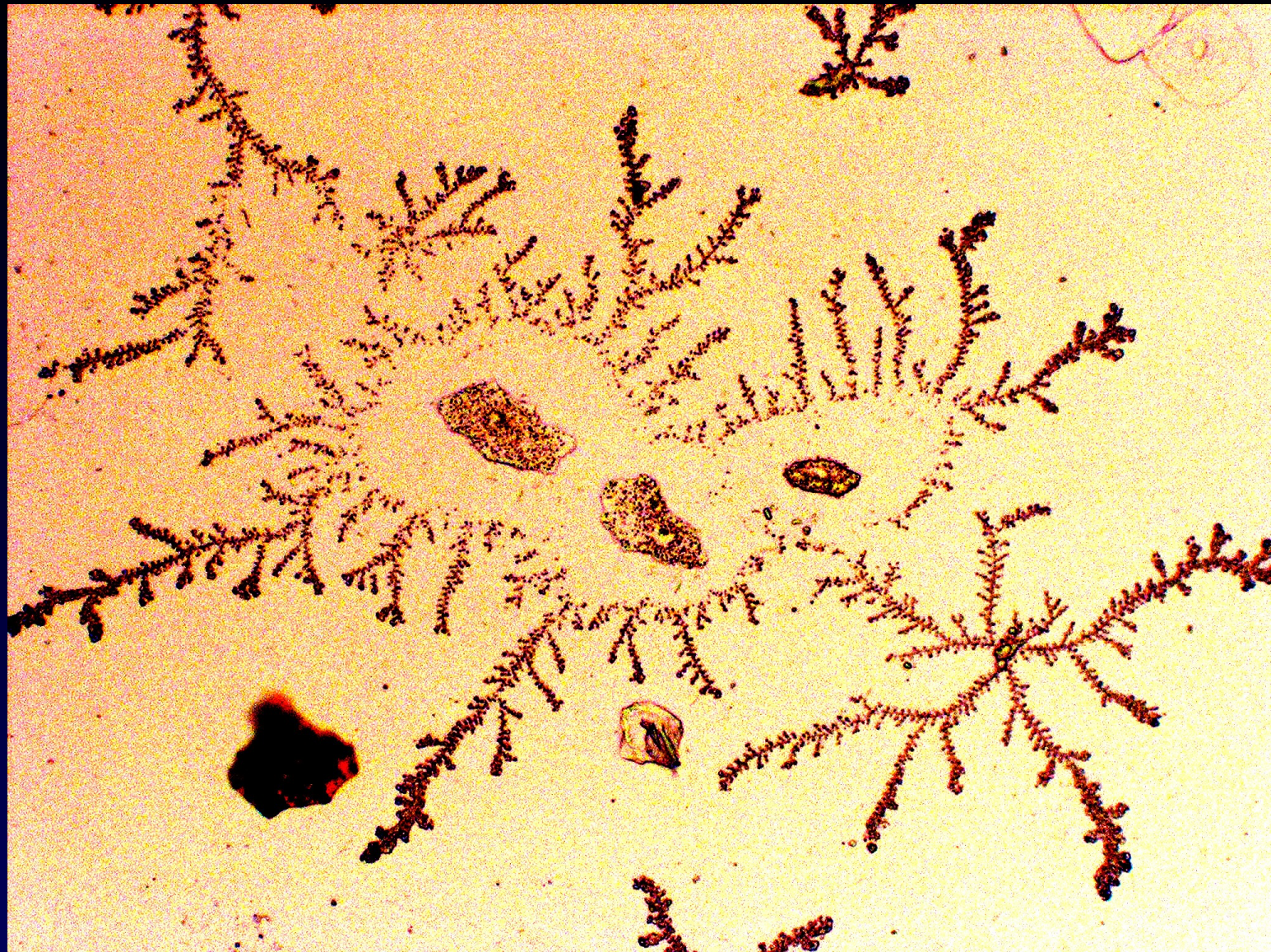
0120 15KV X5,000



1 μ m WD10

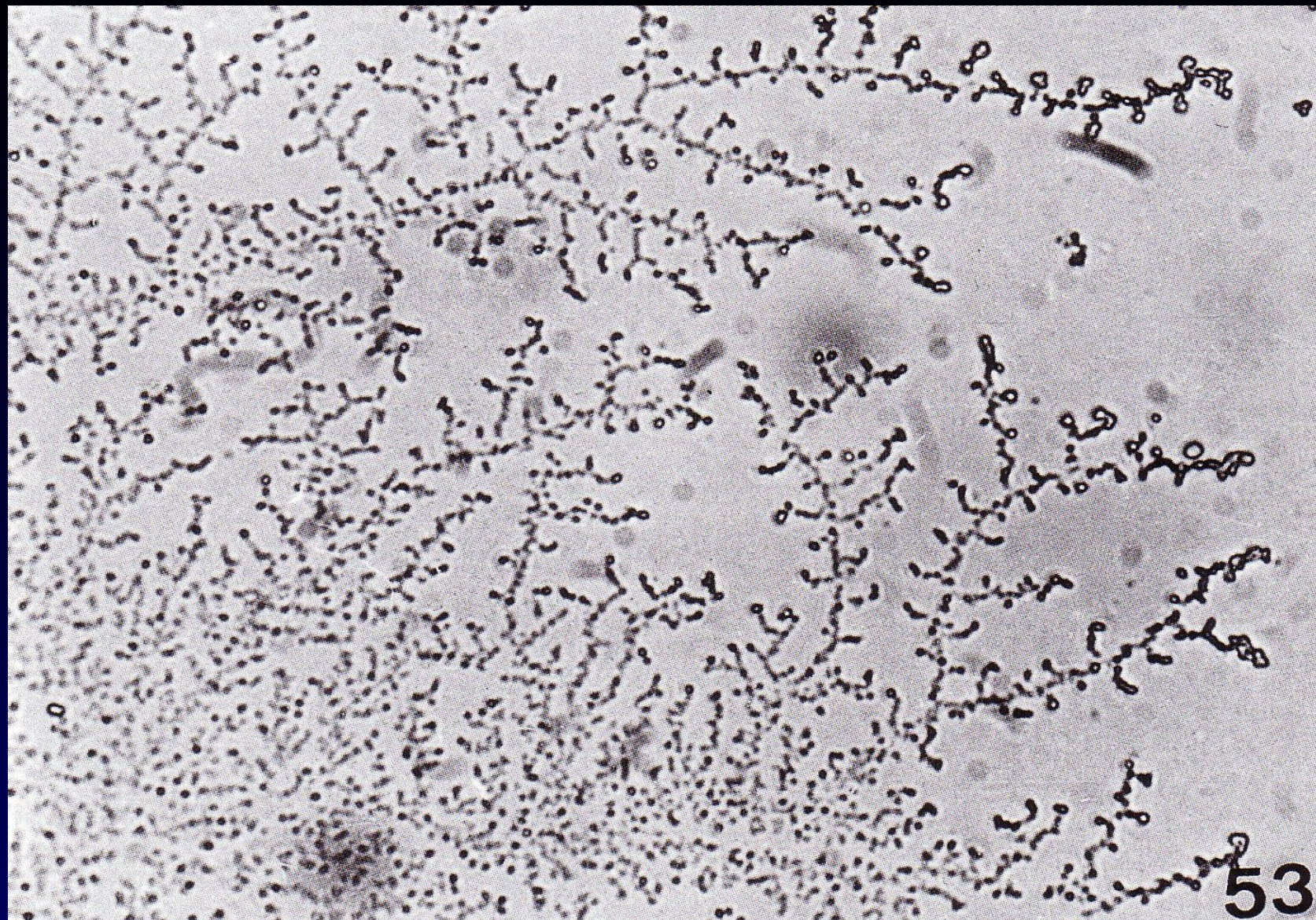






P mucus

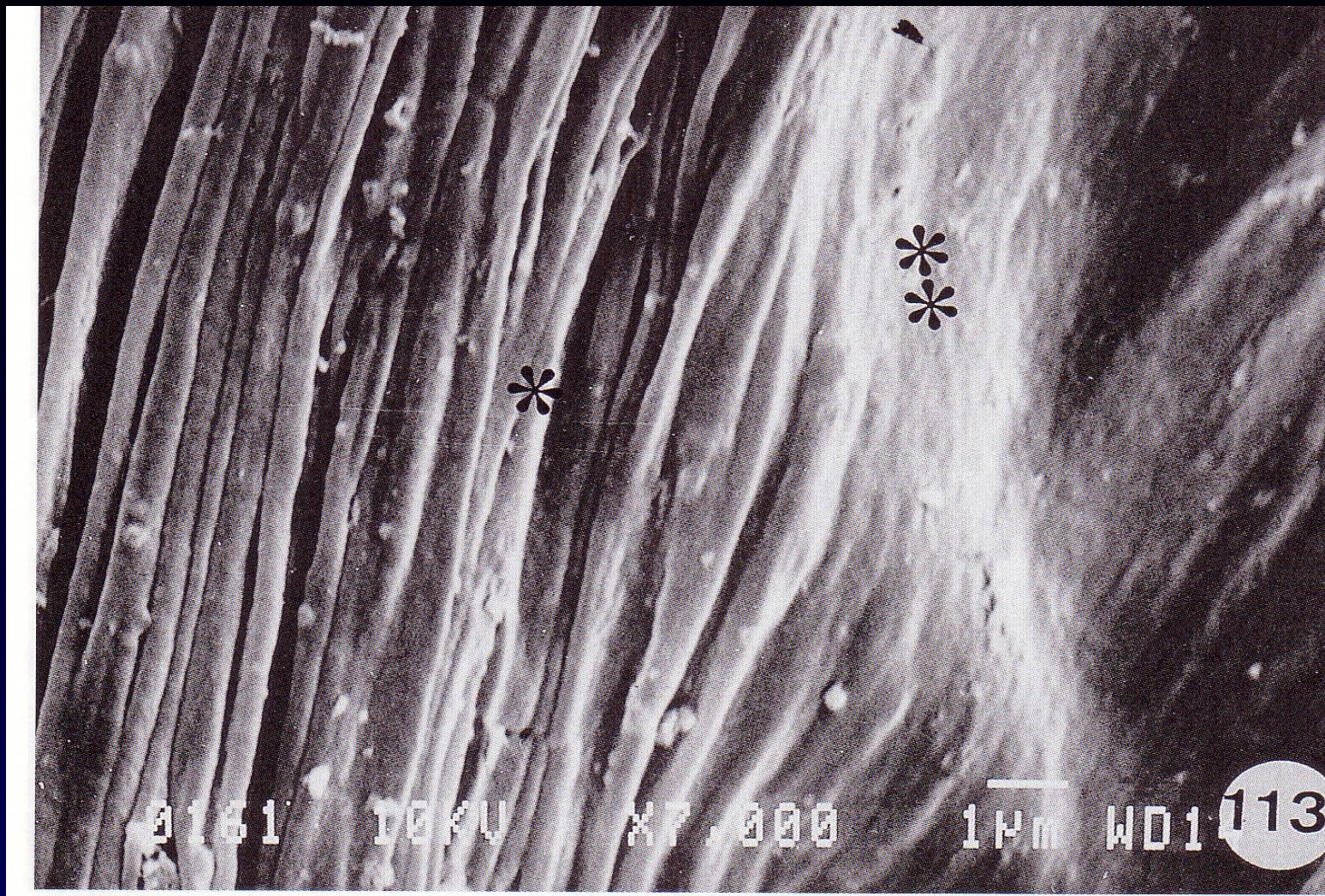
- Pt: consisted of triangular crystals. Both, axis and branches seemed to be formed by crystals, which were not always joined.



53

P MUCUS

- P mucus: P mucus type fixed samples occurred on plain surfaces, tending to form parallel folds. Sometimes pores were also observed on the surface with diameters of 0.4-2 μ m. We could identified this morphology in samples with at least 5% P mucus.



0181

TEKV

XP,000

1µm

WD1

113

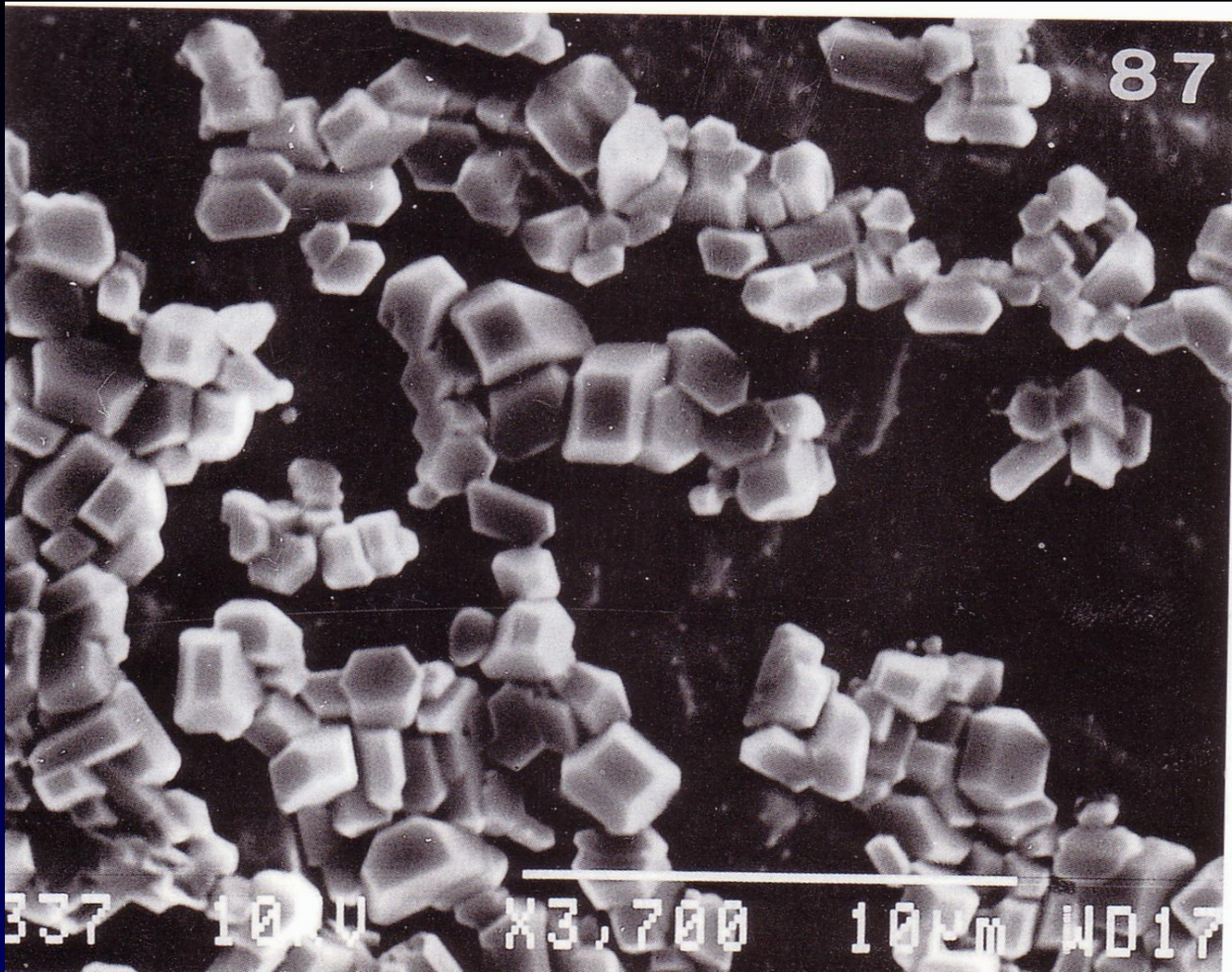
G MUCUS

G MUCUS: gestagenic; first and second infertile phases of the cycle.

- G mucus: the G mucus consisted of free crystals with a different morphology and some times a large number of cells.

87

337 1000 X3,200 10µm WD17



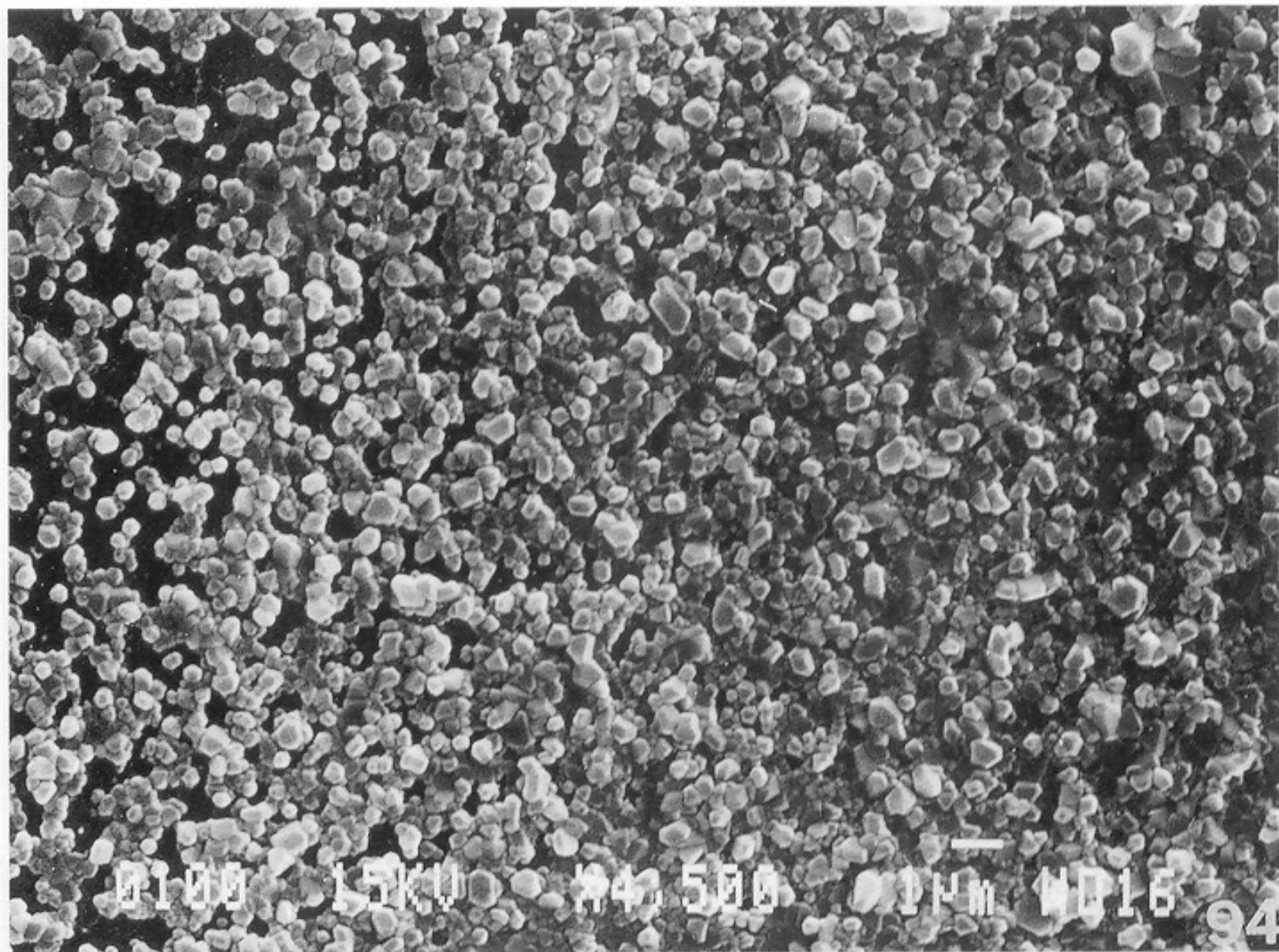
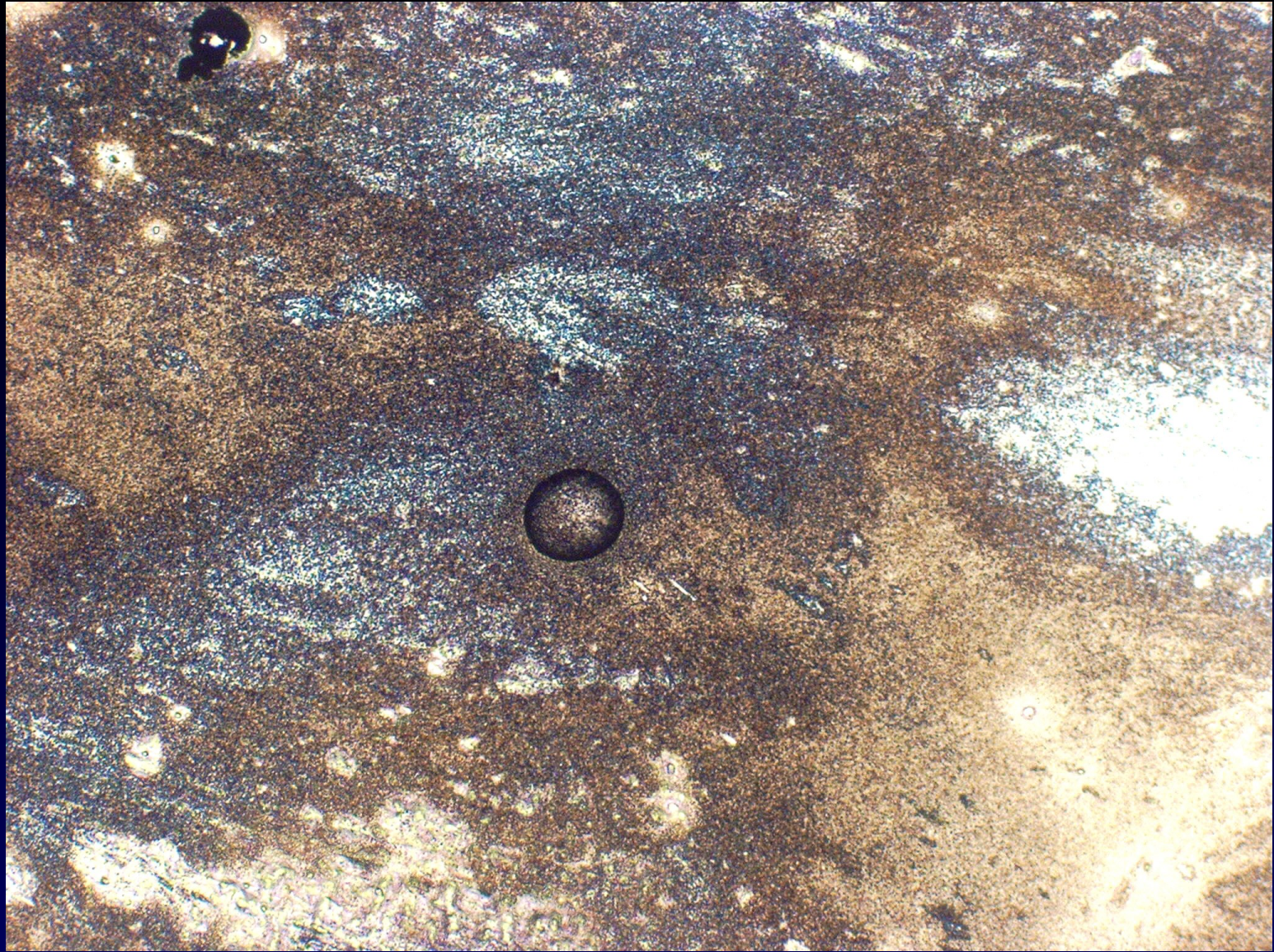


Fig. 94. Al observar los cristales con más aumento vemos una gran densidad de ellos, sin organización entre sí. Muestra cripta G. MEB x 7875.



G MUCUS

- In the G mucus fixed samples, it presented large plain surfaces and sometimes red blood cells or other cells. With a high magnification we were able to see the pores (0.1-0.5 μ m).



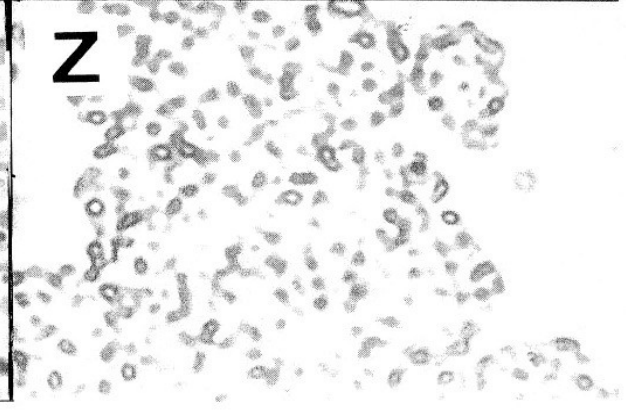
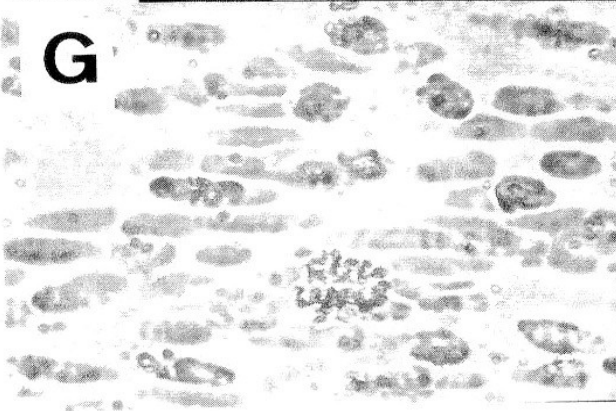
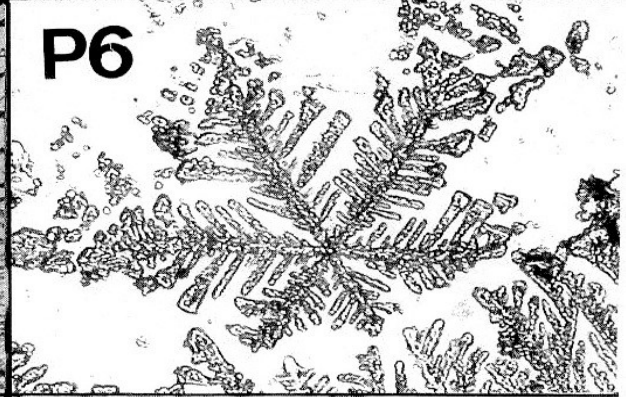
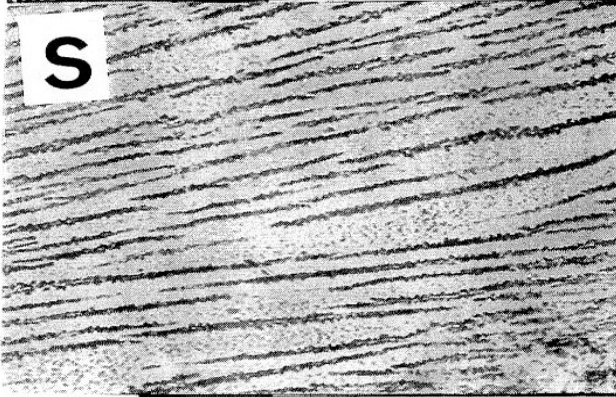
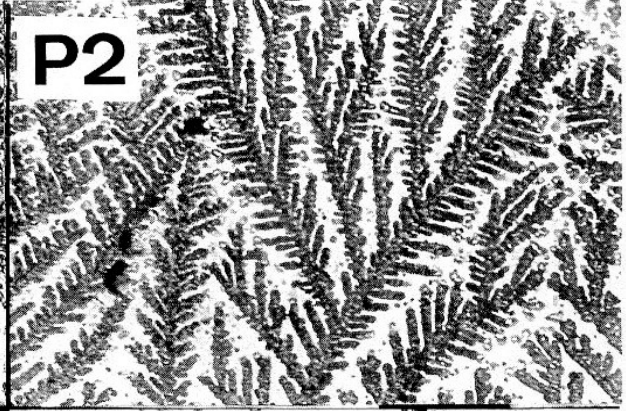
0286

10KV

X1,500

10µm

WD118



Cervical secretion

- These four mucus types are produced in different and specific crypts in the different areas inside the cervix.

Types of secretion

Z

P₂ or P₆

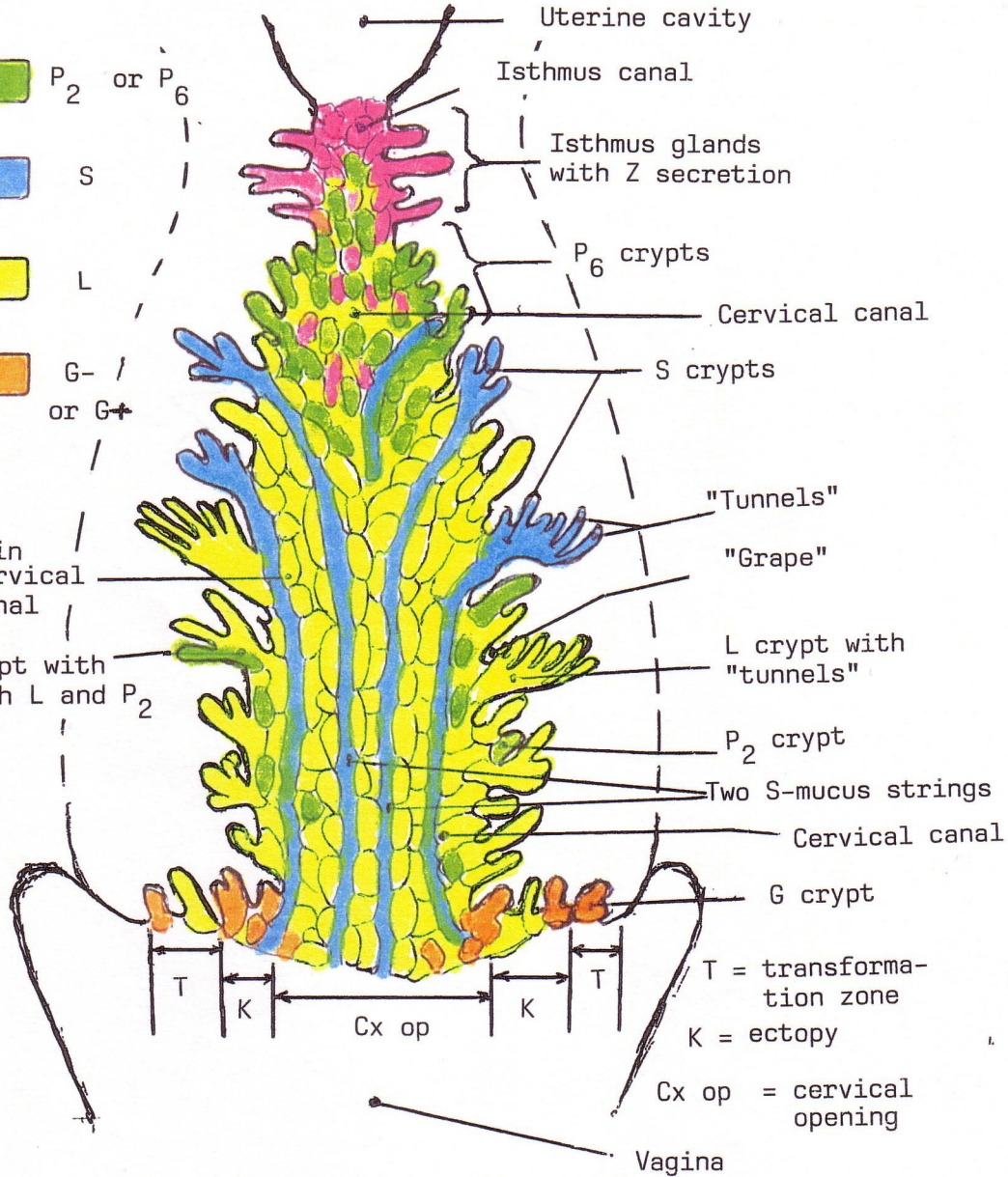
S

L

G- /
or G+

L in
cervical
canal

Crypt with
both L and P₂



Cx op

Cx op = cervical opening

Cervix

- In a non pregnant woman, aged 25-30 and not having used contraception, the cervix is 22 mm long (average) and the average diameter is 6mm at ovulation time. The crypt distribution starting from below and going upwards is as follows: the G crypts dominate in the lowest 4 to 5mm.

Cervix

- Then, there is a zone of L crypts, occupying the next 9-10mm, followed by the S zone, for 5-6mm. The highest three to four mm contains the P crypts. The borderlines between the zones are not clearly defined; there is some overlapping.

Types of secretion

Z

P₂ or P₆

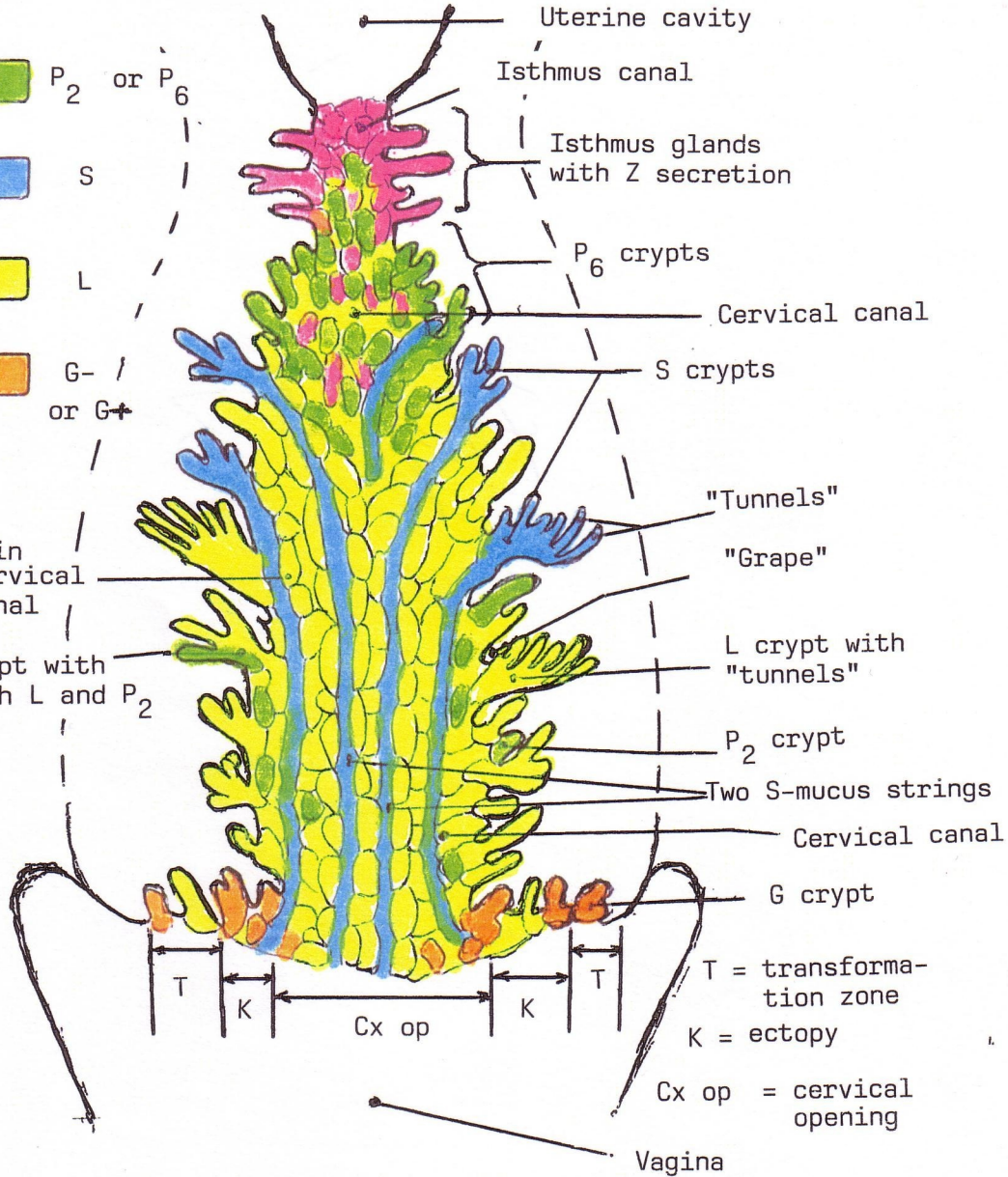
S

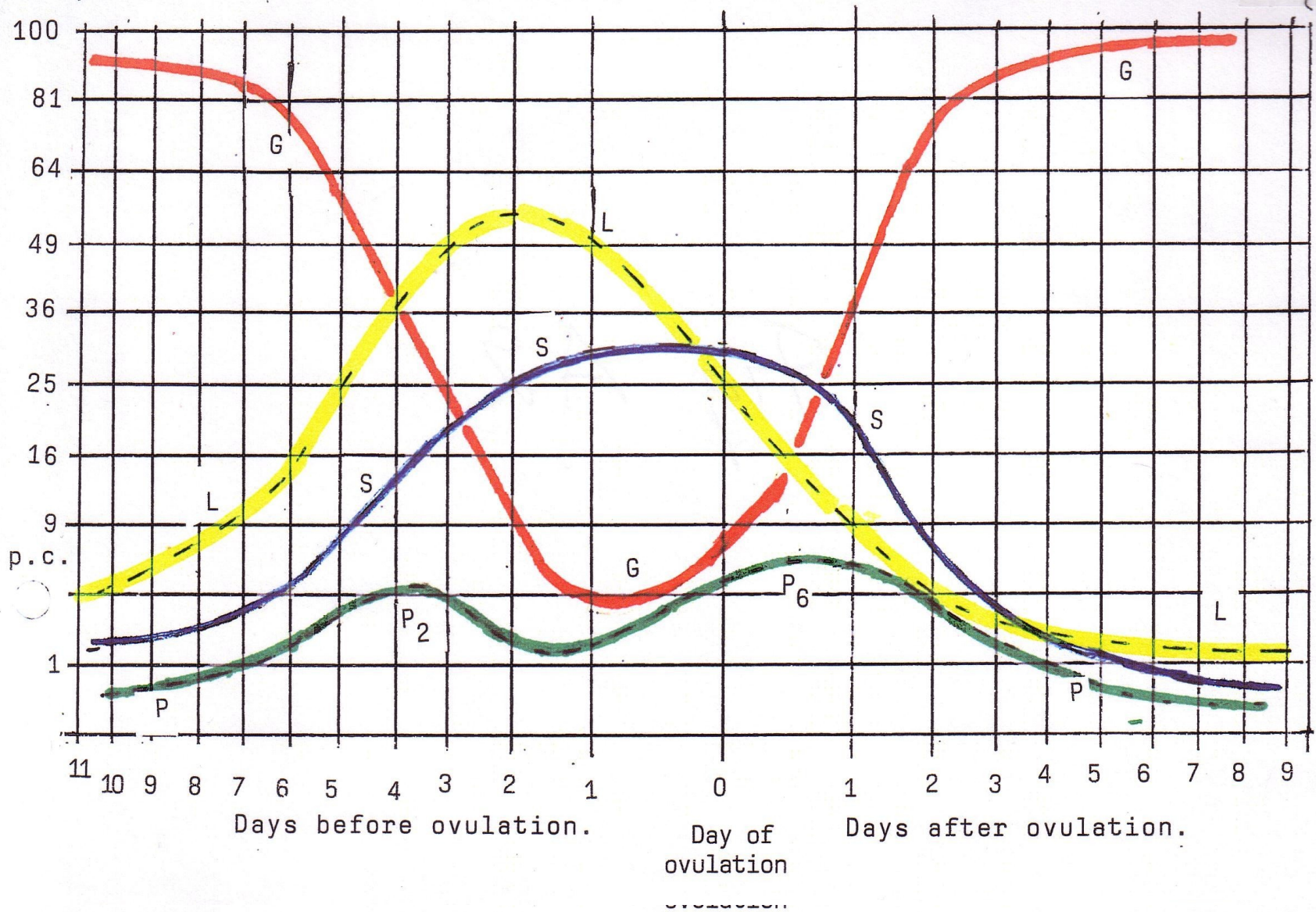
L

G- /
or G+

L in
cervical
canal

Crypt with
both L and P₂





Some binary cell-secretion systems in the female genital tract

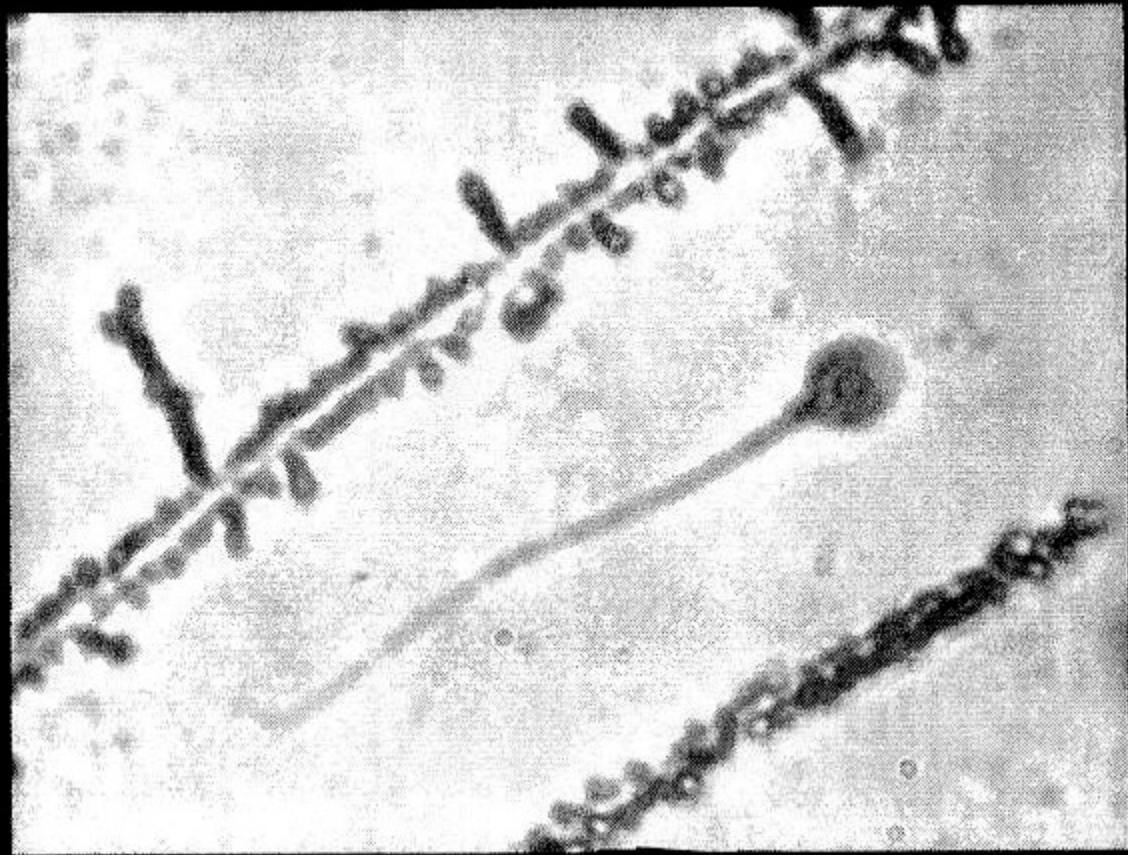
Erik Odeblad, Micaela Menarguez,
Helvia Temprano, Coral Barbas

A single type of cells or a single type of secretion often shows well-defined function.

However, we want to draw attention to systems in which two types of secretions or cells seem to form a symbiotic unit with a meaningful function of importance in the female genital tract.

The first time this became evident was when the sperm propagation in gently prepared cervical mucus was studied.

Rapid swimmers with normal morphology
advanced within the S mucus string.



But slow swimmers with abnormal shape
deviated laterally into the L mucus
surrounding the string.

1) So the first conclusion is that the intimate contact of the two mucus types, S and L, is necessary for the sperm selection.

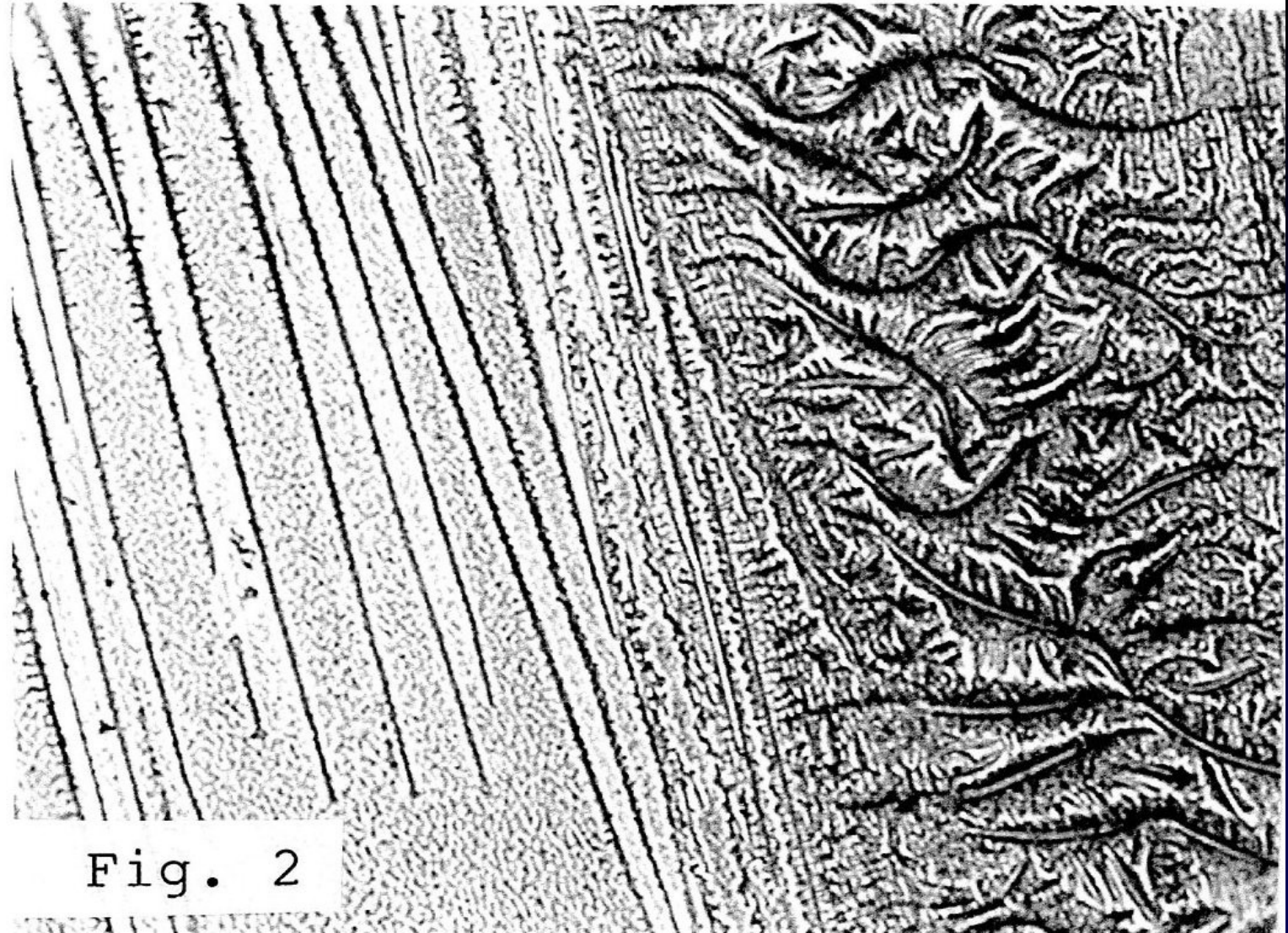


Fig. 2

Interactions between S and P6 mucus and between S and Pt (the immediate precursor of P6 mucus type) are very common.

They form broom-like structures in the spread-out dried smears of mid-cycle cervical mucus.

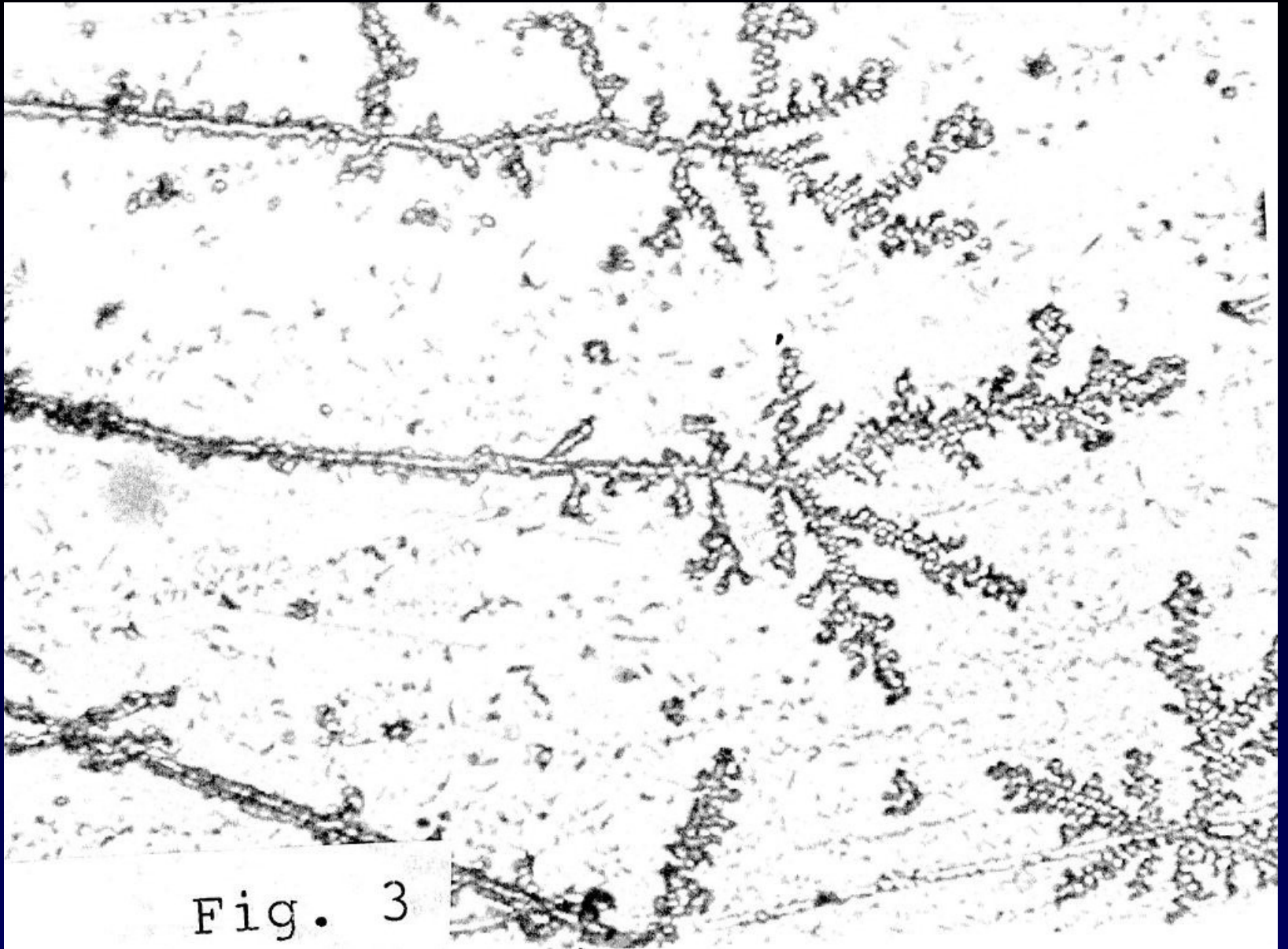
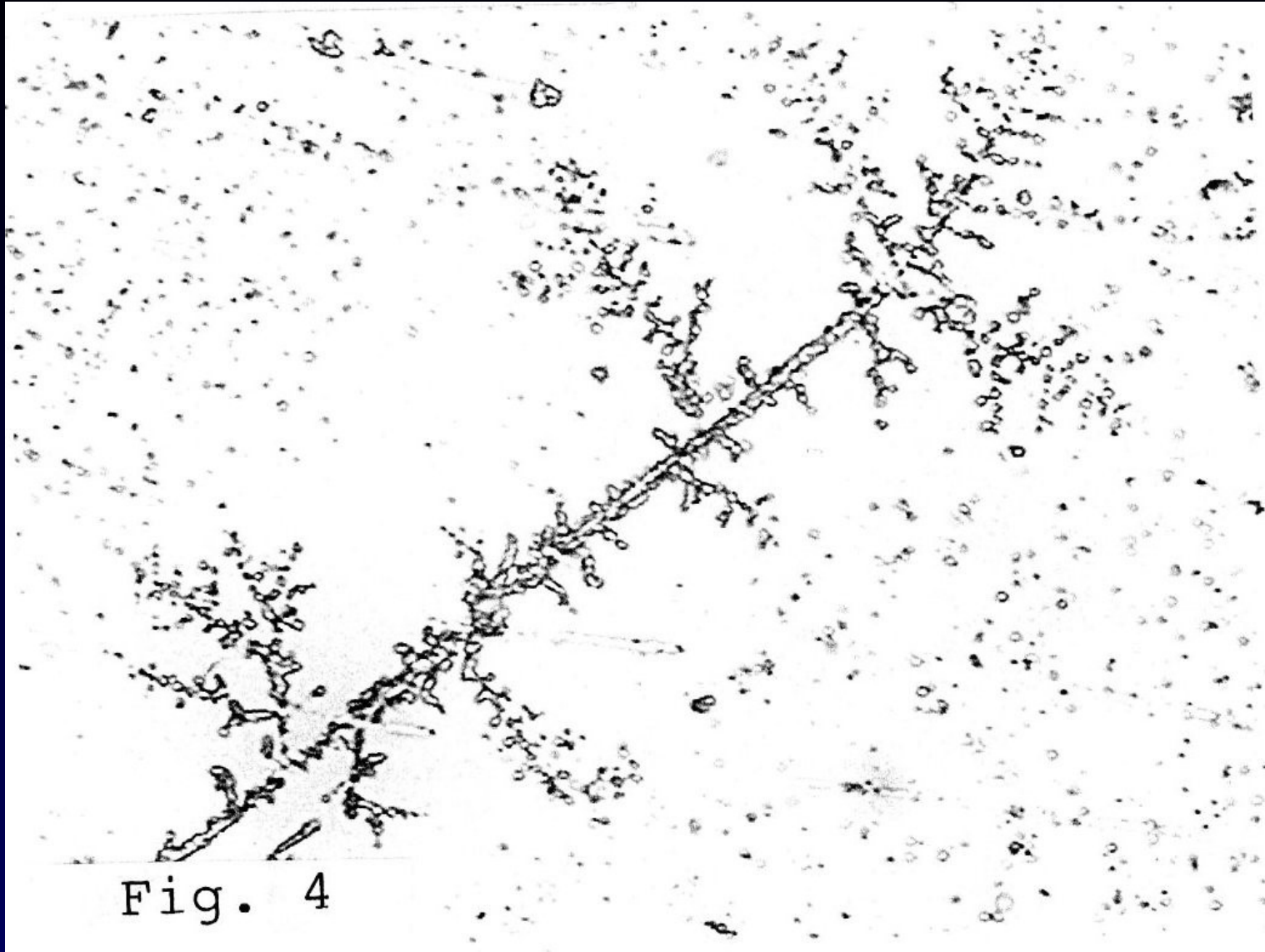


Fig. 3





2) The function of these brooms in vivo are not yet understood, but second conclusion could be that they may also contribute to sperm selection.

Another common structure in mucus smears are the so-named grain drops, GD.

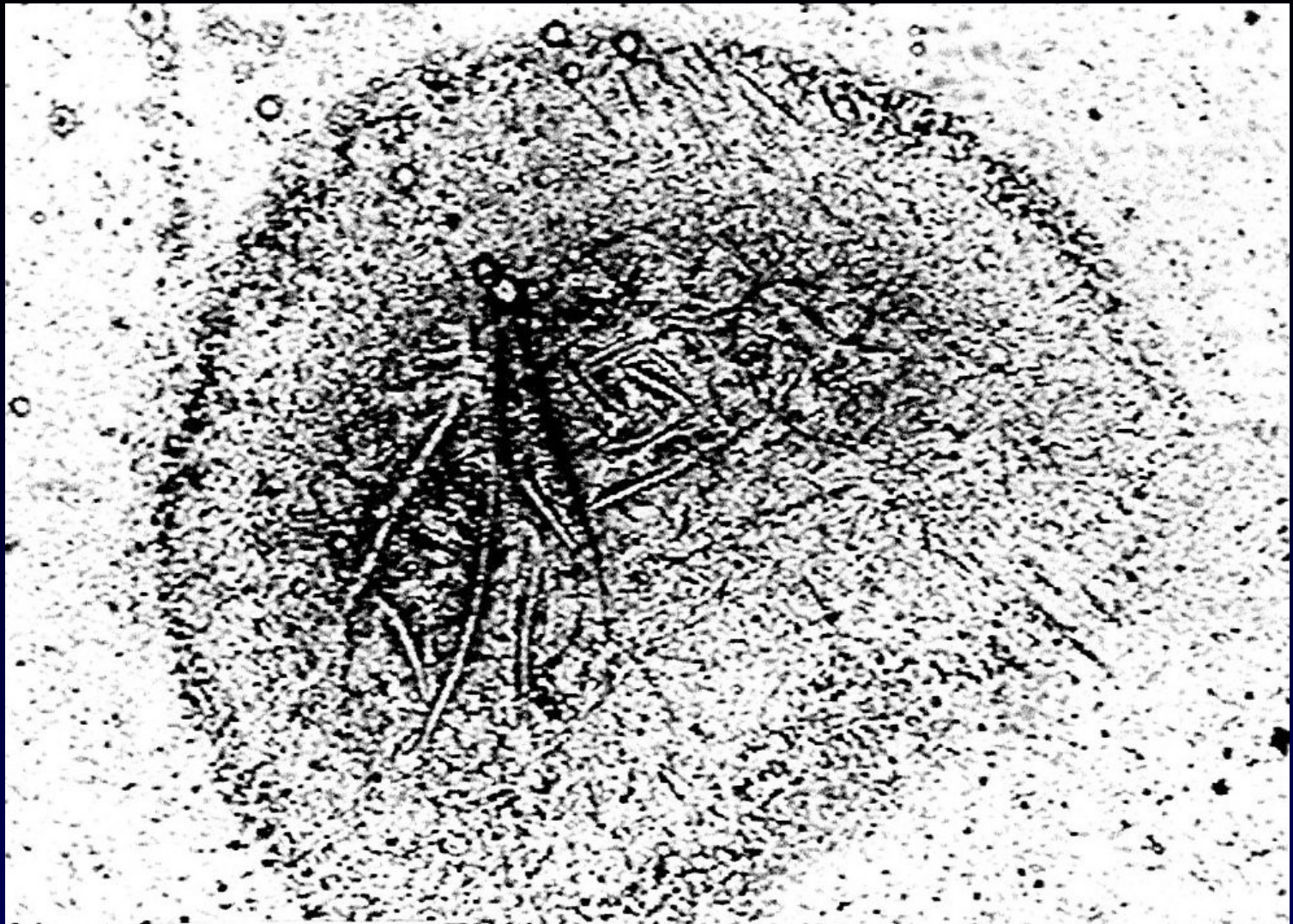


Fig. 5

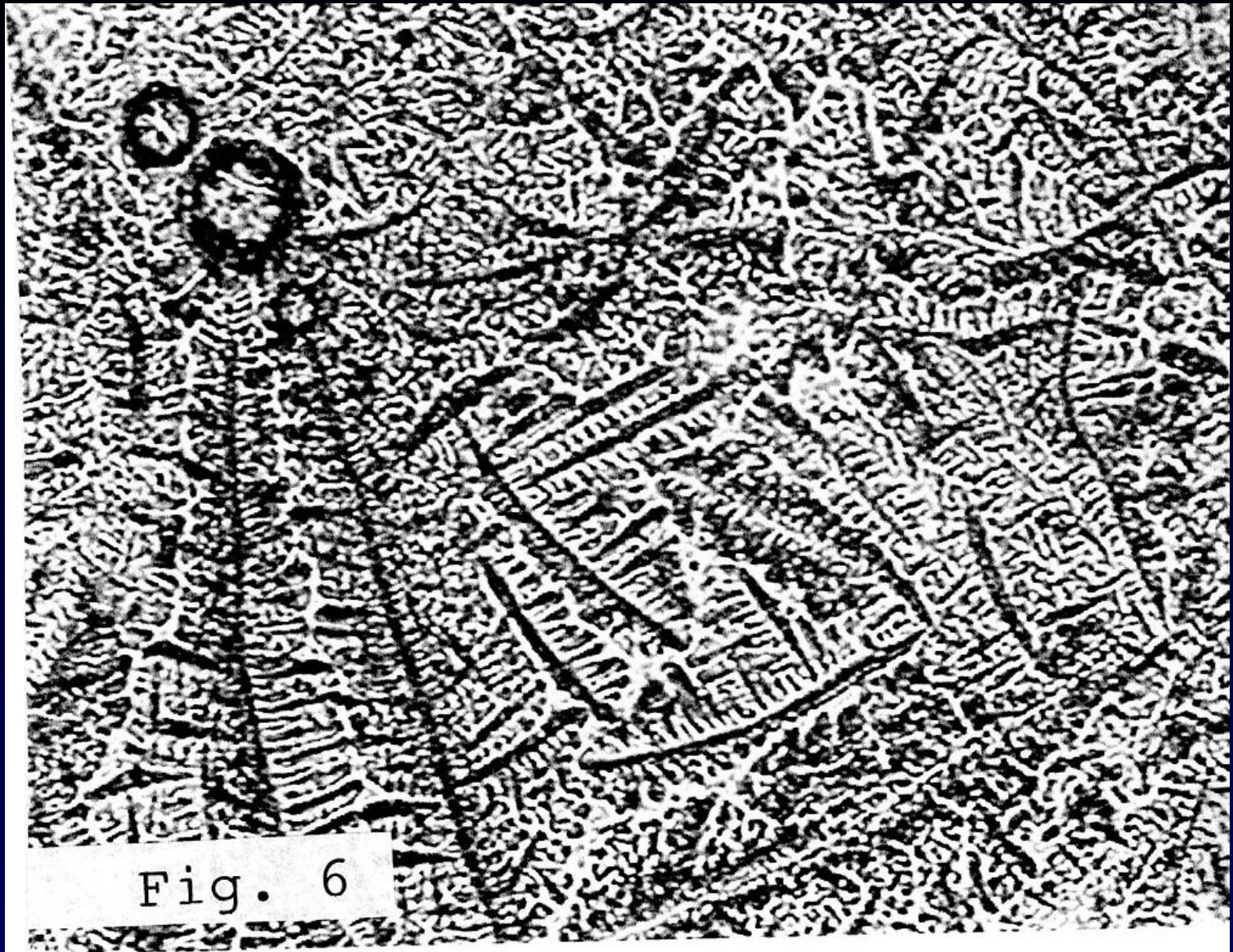


Fig. 6

In a smear of an area of a few cm², they may be found in 4 to 9 numbers.

They look-like a collection of thousands of grains of micrometer size, the whole drop may be 0.3 – 1mm in diameter.

A more careful observation reveals a crystalline center, the crystals resembling L mucus, but may be some other mucus not yet identified.

3) Because de GDs are so common, they might have some function, perhaps mucolytic function, between GDs and cervical mucus, which we are now studying.

Grains together with crystals are also
found in the P2 mucus.

It has been possible to follow P2 mucus
from upper to lower cervix.

In the lower part of the cervix, near the cervical opening, the P2 mucus units are surrounded by watery contents suggesting mucolytic activity.

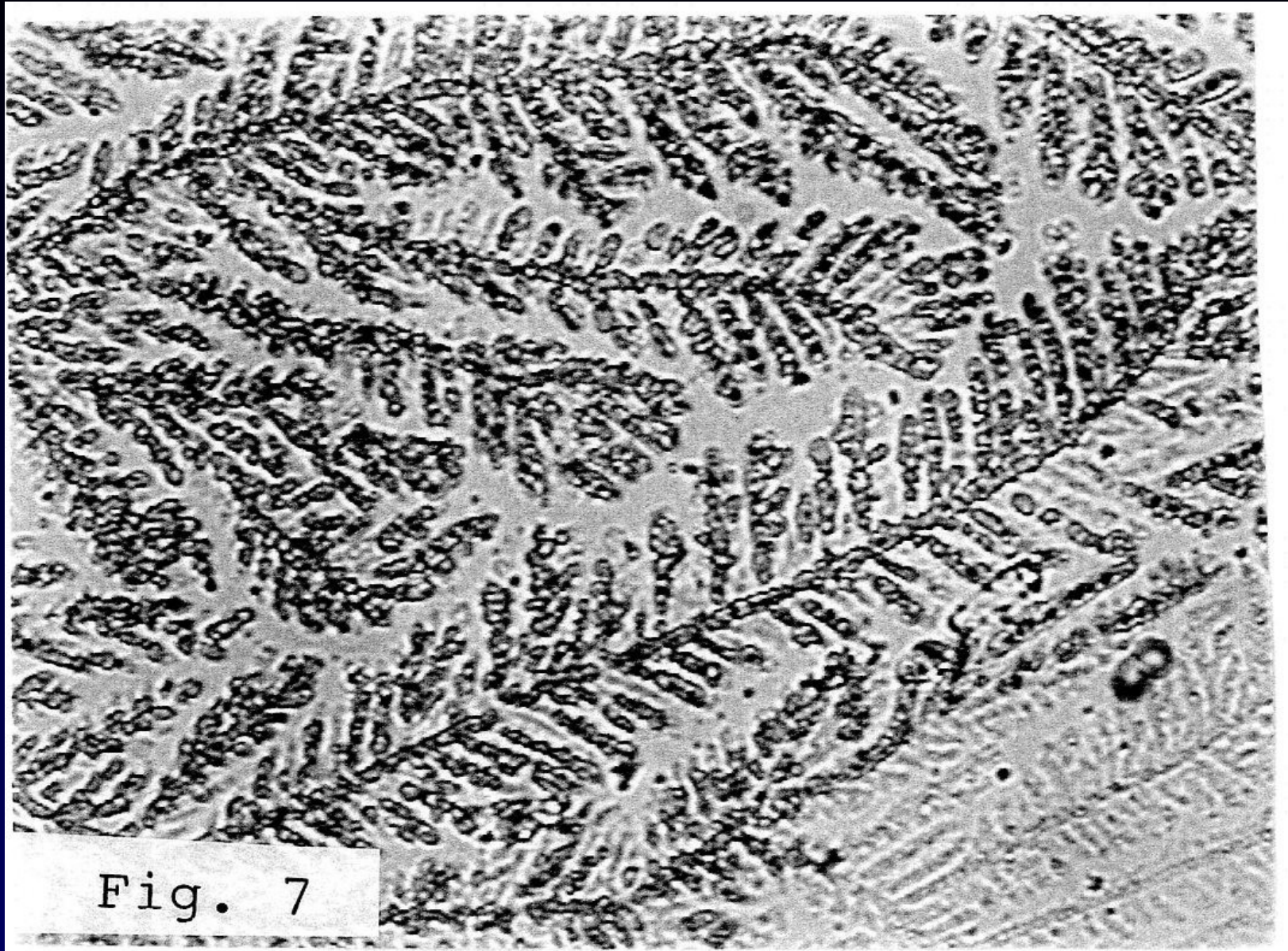


Fig. 7

4) Forth conclusion should be that this mucolytic process occurs early in the fertile period and may help to “clean” the cervical canal from G mucus and be ready to hold the L and S secretions.

The peak symptom depends largely on the secretion of, first, the L, and then, both, L and S, and finally S and P6 mucus types.

The peak symptom is not experienced in the cervix and not in the vagina, but in the vestibular part of the vulva.

Therefore smears have been removed from the vestibular area and examined in the microscope. Small quantities of L and S mucus have been found, but P6 dominates.

Also another type of structures were seen, the “rope-like objects”, R L O-s.

These could be finally be explained as
the result of normal apoptosis
(programmed cell dead) of the surface
cells of the vestibulum.

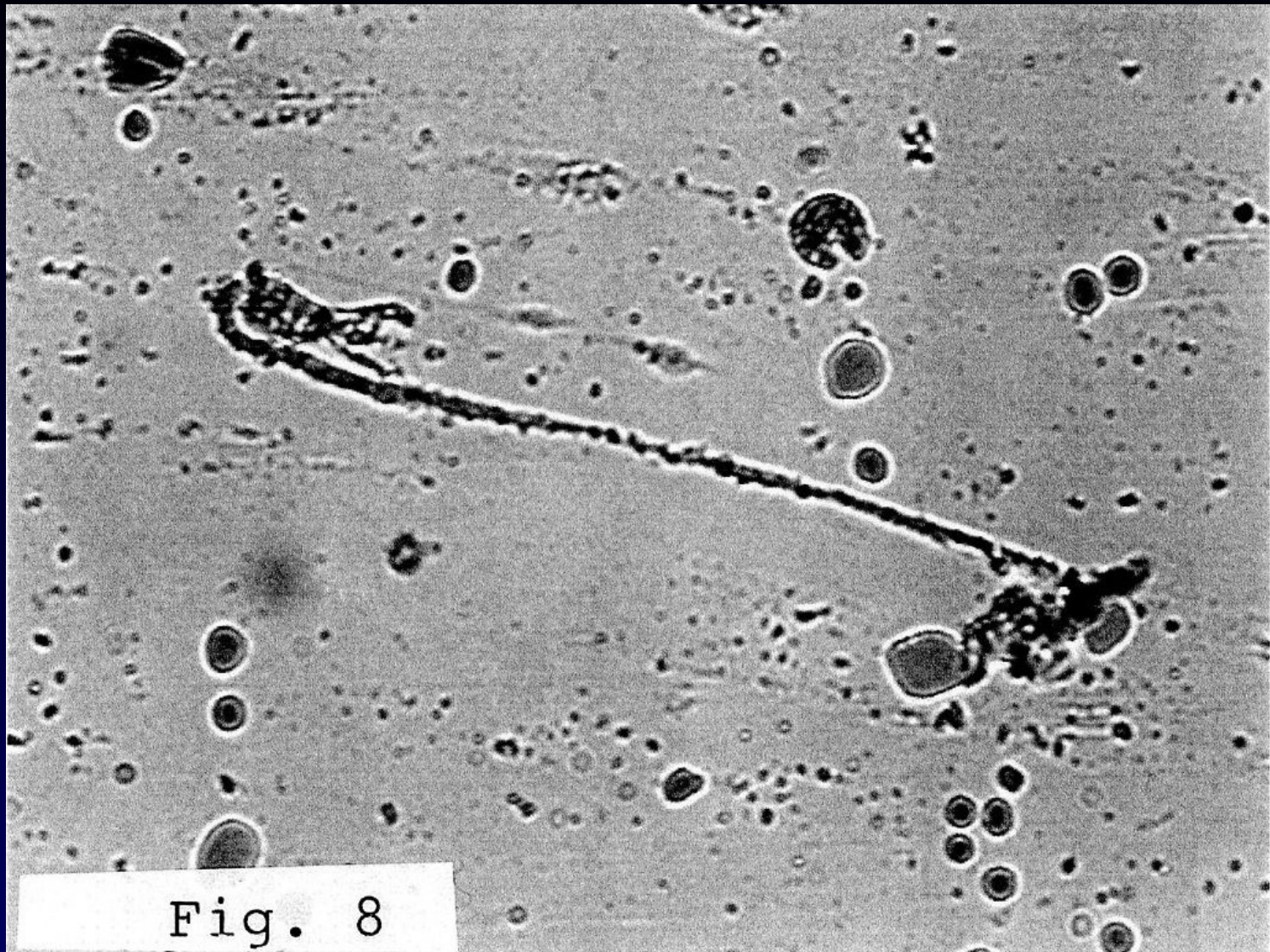


Fig. 8

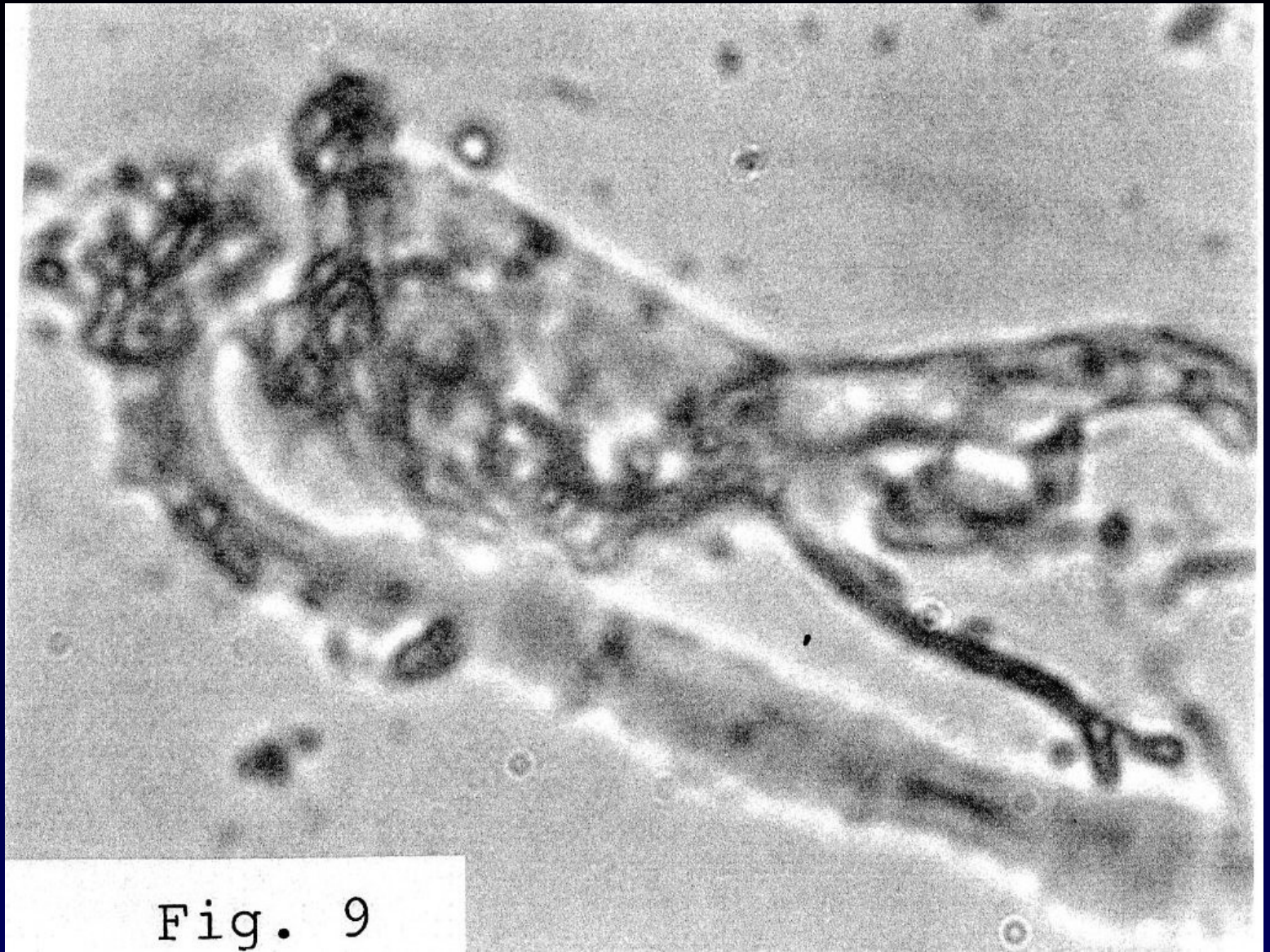


Fig. 9

In the photos before, we can observe how this apoptosis gives rise to elongated cell residues (ropes), apparently with great affinity for P6 mucus which enhances the slippery peak sensation.

5) Both together, P6 and cell residues, enhance the slippery peak sensation and helps women to identify ovulation.

After the peak, in the postovulatory phase, the G mucus dominates and fills the cervical canal. This has been considered to be a trivial part of the cycle, but recent findings have made it more interesting.

P cells with a very low secretory activity, have been found in the G mucus.

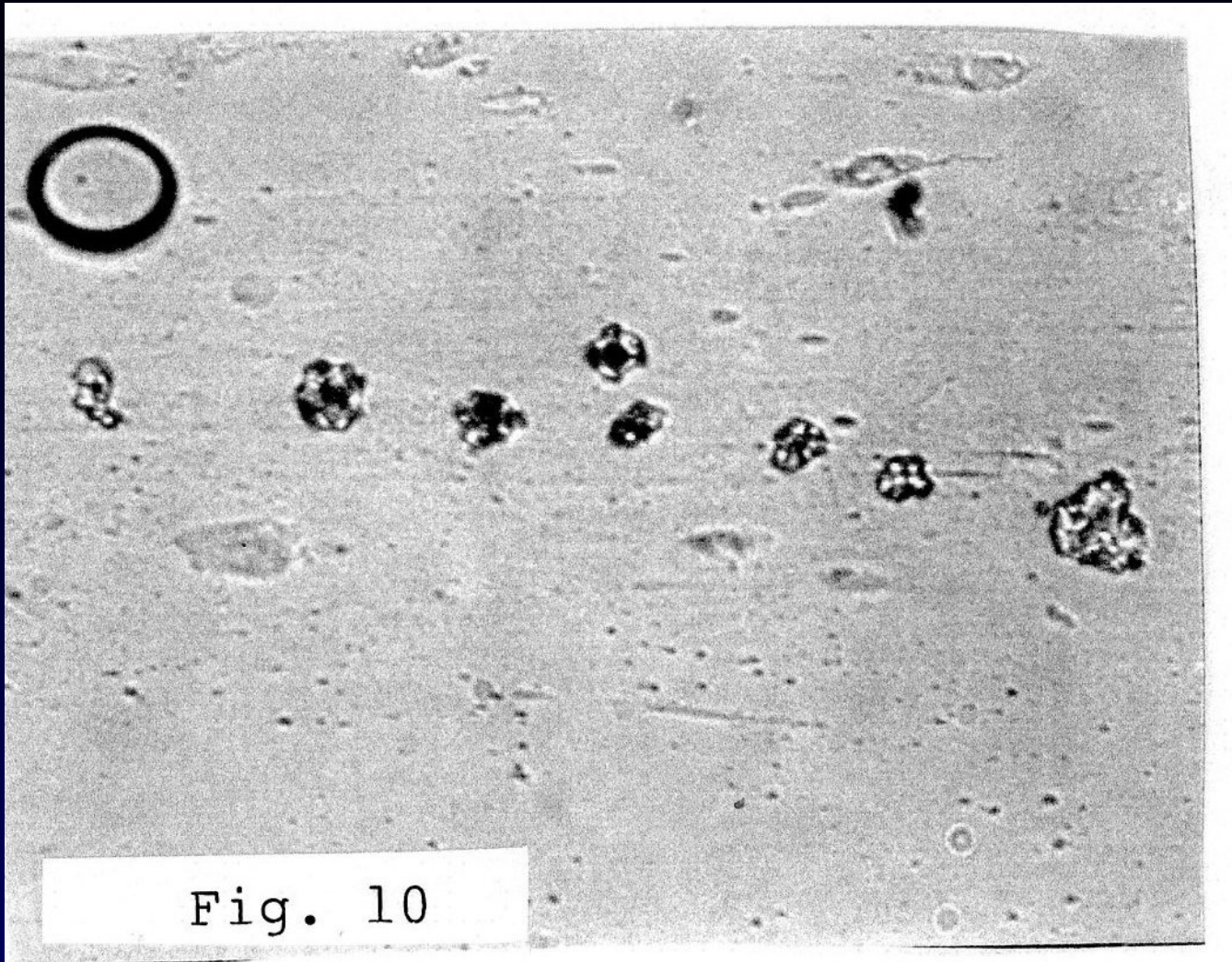


Fig. 10

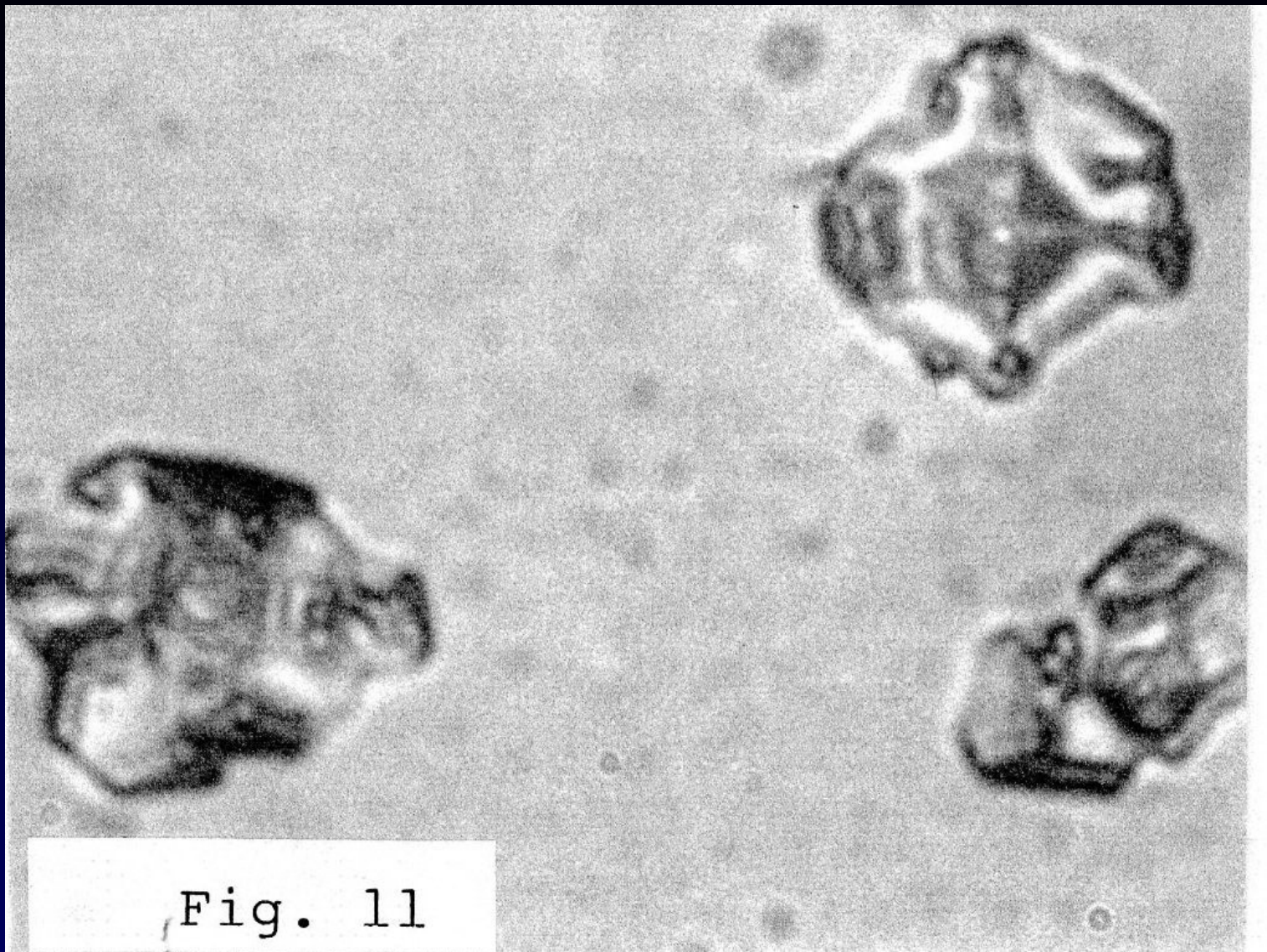


Fig. 11

Series of studies indicate that these cells persist until and after the next menstruation, when they start to be active and later, develop to P1, P2, P4 y P6 cells.

As long as they are dormant, they are inactive (they do not receive enough of oxygen, ATP, etc..within the G mucus.

6) This is an illustrative example of “team work” between a secretion (G mucus), and cells (P cells).

Probably in the future more of these binary systems may be found helping to understand more of the human reproductive physiology.

Fig. 1.

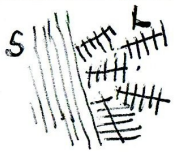

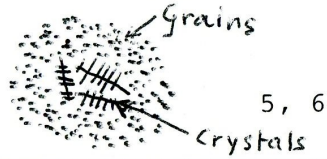

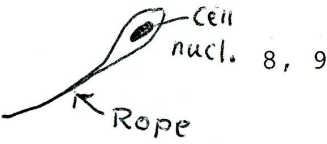
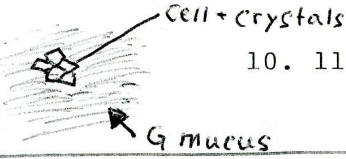
Microscopic object	Abbrev.	First descr.	Schematic drawing	Fig. in this paper	Site of production	Remarks Function
boarderline L - S		Verbal Mel- bourne 1983		2	CERVICAL CANAL	Removing unsuitable sperm
Brooms		This paper		3, 4	Cervical canal	Sperm sorting?
Grain drop	GD	1997		5, 6	Cervical canal	Unknown
P2 + grains		1992		7	Cervical canal	Mucolytic grains from isthmus
Rope-like objects	RLO	2008		8, 9	Vestibulum	Increase peak sensation
Inactive Pn cells in G mucus	Pni	Odeblad, this congress		10. 11	P cell line and G crypts	Keep Pn-cells inactive until next cycle.

TABLA I

Table I

Cell type	Type of mucus	Cells				Enzyme grains	Crystals			
		Leuco-cytes	Lymph-cytes	Epithel. cells	Sperm 12 h. p.c.		Rect-angular	Hexagonal	Parallell needles	Irregu-lar
G	G-	++	++	++	0	+	0	0	0	(+)
	G+	+++	+++	+++	0	+	0	0	0	(+)
L	L	(+)	0	0	+	+	+++	0	0	0
S	S	0	0	0	++	+	0	0	+++	0
P	P6	(+)	0	(+)	+	+	0	+++	0	0
	P2	(+)	0	(+)	0	+++	0	+++	0	+
Z	—	0	0	(+)	0	+++++	0	0	0	0

CONCLUSIONS

CONCLUSIONS

- Human cervical mucus located inside the cervical canal is a morphological heterogeneous entity with different types of secretion, the percentages of which vary during the cycle. They show a different ferning and ultrastructure, related to the arrangement of the glycoprotein network, and are produced in different zones of the crypts in the cervix

Morphological characterization of
different human cervical mucus types
using light and scanning electron
microscopy.

M.Menárguez, L.M. Pastor and
E. Odeblad.

Human Reproduction Vol. 18, No 9 pp
1782-1789, 2003 (cover front)

CONCLUSIONS

- What is surprising in this investigation is to observe the care that Nature has bestowed upon the selection and filtering of sperm, being extraordinarily generous with the number of spermatozooids secreted in each ejaculation (400-500 million; all european union population together).

CONCLUSIONS

- Later, it puts them through a large number of these and difficulties in advancing...





CONCLUSIONS

- At the end, only one of them, the best...



FINAL CONCLUSION

- ... is responsible, together with the ovule, for the generation of a new human life.



“ We would like to emphasize that the cervix is an organ of great biological complexity and very precise functions. It is sensitive to infections and external factors, such as the effects that hormonal treatments often carried out without adequate medical control, produce it.

The maintenance of reproductive health in the female should also consider these questions. Women have a right of a healthy cervix, as part of their reproductive health, and our investigation pretends, as far as possible, to help them to achieve it”
(Prof. Odeblad)





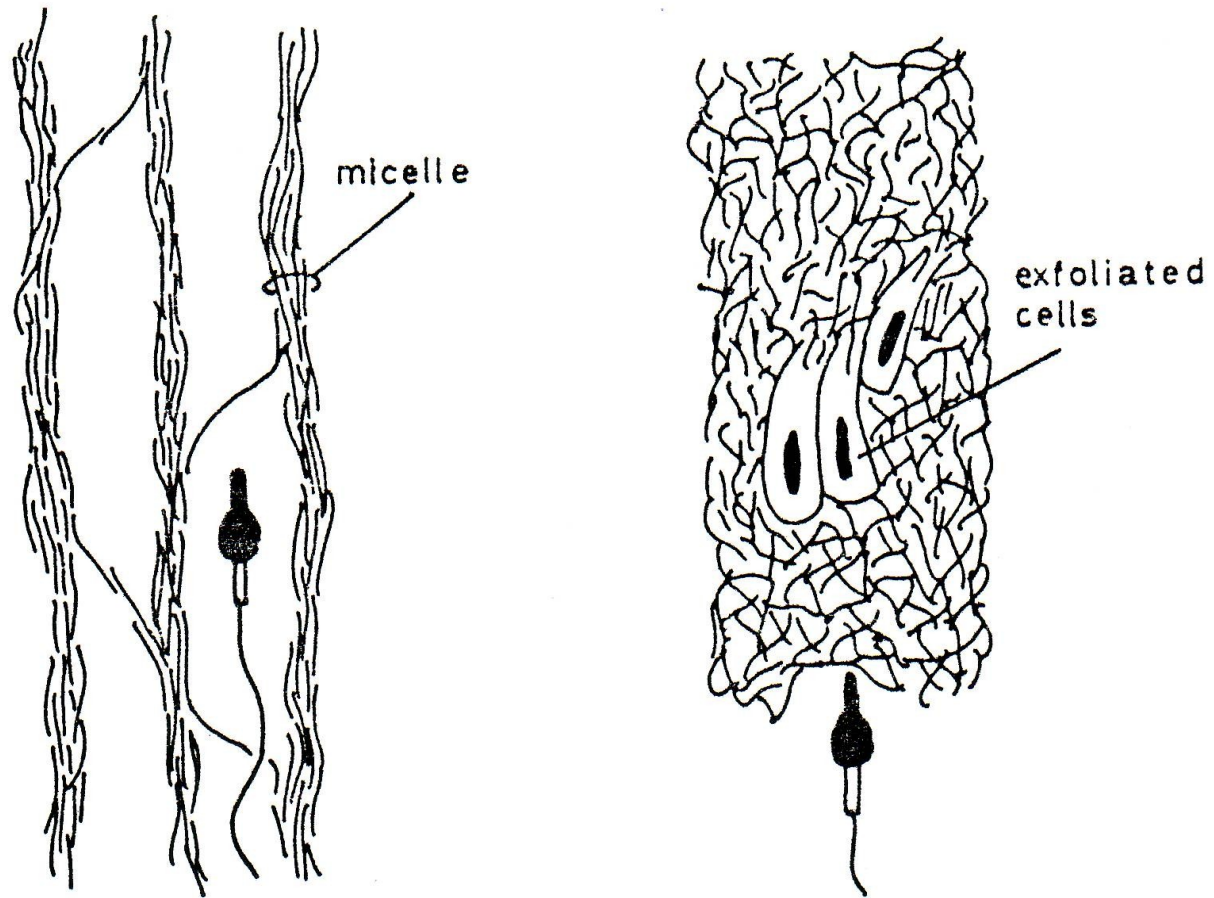


Diagrama 16. Modelo que muestra las características del moco estrogénico, a la izquierda, y el gestagénico, a la derecha. El modelo de la izquierda indica la micelas y los espacios intermicelares, con un espermatozoide. El modelo de la derecha muestra la densa red, sin estructura micelar, que impide el paso de los espermatozoides (Odeblad, E. The functional structure of human cervical mucus. Acta. Obst. Gyn. Scand. 47. (Suppl. 1). 58-79. 1968 a).

