Aspects macroscopiques et microscopiques d'intérêt dans les placentas gémellaires

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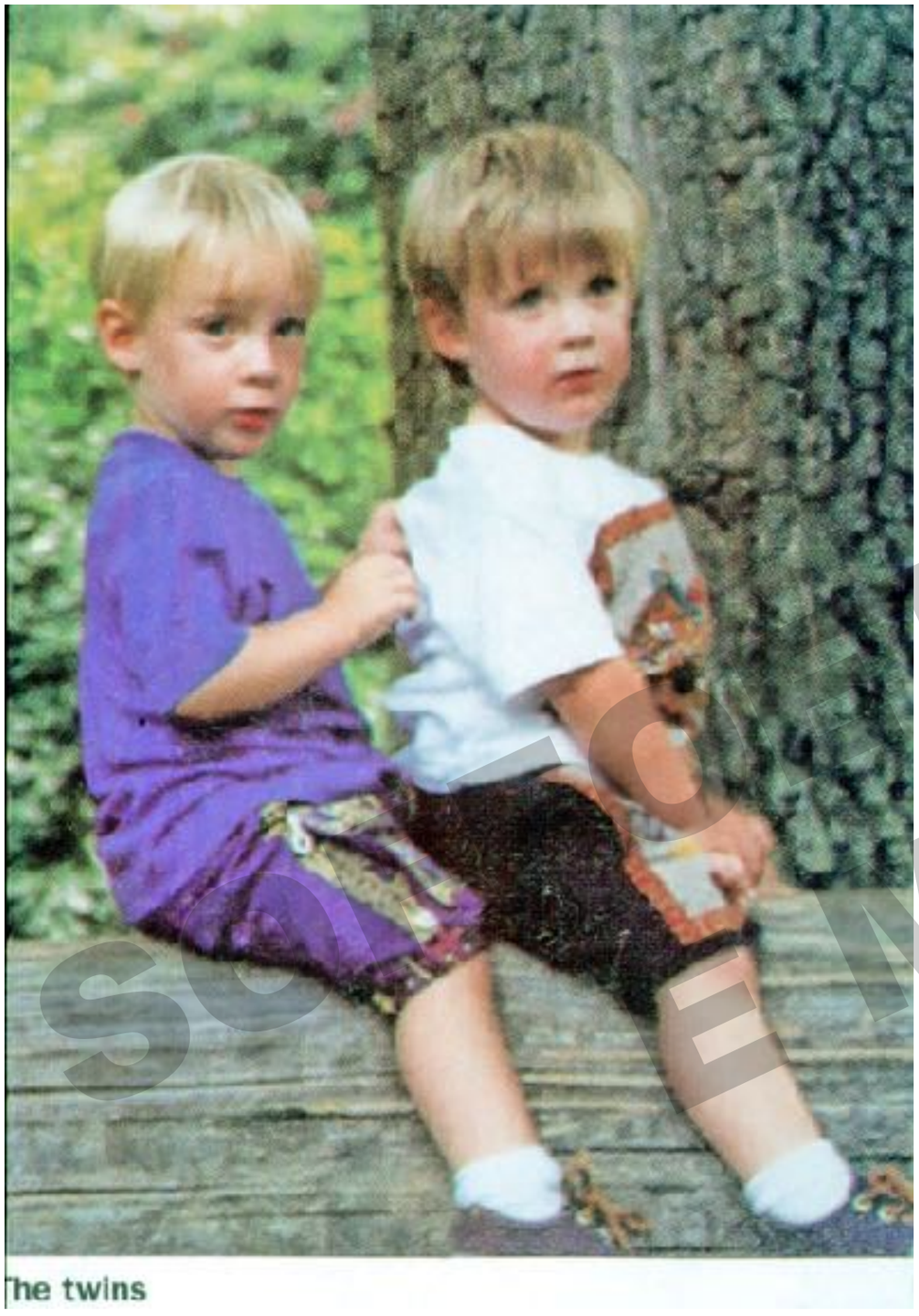

The twins

Identical differences

Paul Gringras

1-year-old male twins attended the Multiple Births Foundation twins clinic for routine developmental review. They had been born at 35 weeks' gestation with a 15% discordancy in birthweight and placental histology which confirmed a monochorionic, diamniotic placenta with a single arterio-arterial anastomosis. Due to the placental findings the twins were assumed to be monozygous and no further investigations of zygosity were done.

In the clinic the parents' main question concerned the boys' zygosity. The parents pointed out a number of differences between the two which made them doubt that the twins were identical. The twins were of similar weights and the same length. They were easily distinguishable because of their different hair colour (figure). Eye colour was the same although the shape of the eyes was different. They had slightly different shaped ears and their faces were felt by experienced clinical staff to be no more alike than expected in dizygous siblings. Developmentally they had both reached age-appropriate milestones and one had more words than the other. Their teeth pattern differed in both the order and timing of eruption.

Standardised questionnaire assessments which rely on scoring phenotypic similarities suggested the twins were dizygous.[1] Zygosity was therefore rechecked by PCR on cells obtained from cheek swabs. Genotypes for eight highly polymorphic di-, tri-, and tetra-nucleotide microsatellite repeat markers were identical, further supporting a diagnosis of monozyosity (1 in 2700 chance of this result in dizygous twins).

Although most monozygous twins are phenotypically similar, there are some monozygous pairs who are neither phenotypically nor genotypically identical. Assumptions are commonly made about twins' zygosity based either on direct examination of physical features or indirect use of parental questionnaires. In this case both systems would have led to a false diagnosis of dizygosity. Without the details of these twins' placental histology, or if they belonged to the one third of monozygous twins with a dichorionic separate placenta, they would have been misclassified.

Mechanisms for differences in monozygous twins are complex and not fully understood. A wide range of antenatal genetic and environmental influences can cause phenotypic and genotypic divergence.[2] A possible mechanism for discordant hair colours in this case might simply have been an unequal allocation of neural crest-derived pigment-cell percursors to the twins when the twinning event occurred. Discordant skin pigmentation has been described in monozygous twins with chromosomal mosaicism,[3] and heterochromia iridium has been described in monozygous twins by St Clair et al.[4] In this case, immunosuppressive therapy after a renal transplant was needlessly continued for 15 years because dizygosity had been assumed. In their case discussion, the authors of this paper emphasised that the heterochromia discordance must fall "within the acceptable spectrum of monozygous status". This current report shows that even different hair colour can fall within this spectrum, and the term "identical twins" should be replaced by the more accurate term "monozygous twins".

Thanks to staff at the SGDP Molecular Genetics Research Centre Laboratory at the Institute of Psychiatry for zygosity testing, and to Elizabeth Bryan, Geoff Machin, and John Burn for advice.

1 Bonnelykke B, Hauge M, Holm N, Kristoffersen K, Gurtler H. Evaluation of zygosity diagnosis in twin pairs below seven years by means of a mailed questionnaire. *Acta Genet Med Gemellol* 1989; **38:** 305–13.

2 Machin GA. Some causes of genotypic and phenotypic discordance in monozygotic twin pairs. *Am J Med Genet* 1996; **61:** 216–28.

3 Wulfsberg EA, Wassel WC, Polo CA. Monozygotic twin girls with diploid-triploid chromosome mosaicism and cutaneous pigmentary dysplasia. *Clin Genet* 1991; **39:** 370–75.

4 St Clair DM, St Clair JB, Swainson CP, Bamforth F, Machin GA. Twin zygosity testing for medical purposes. *Am J Med Genet* 1998; **77:** 412–14.

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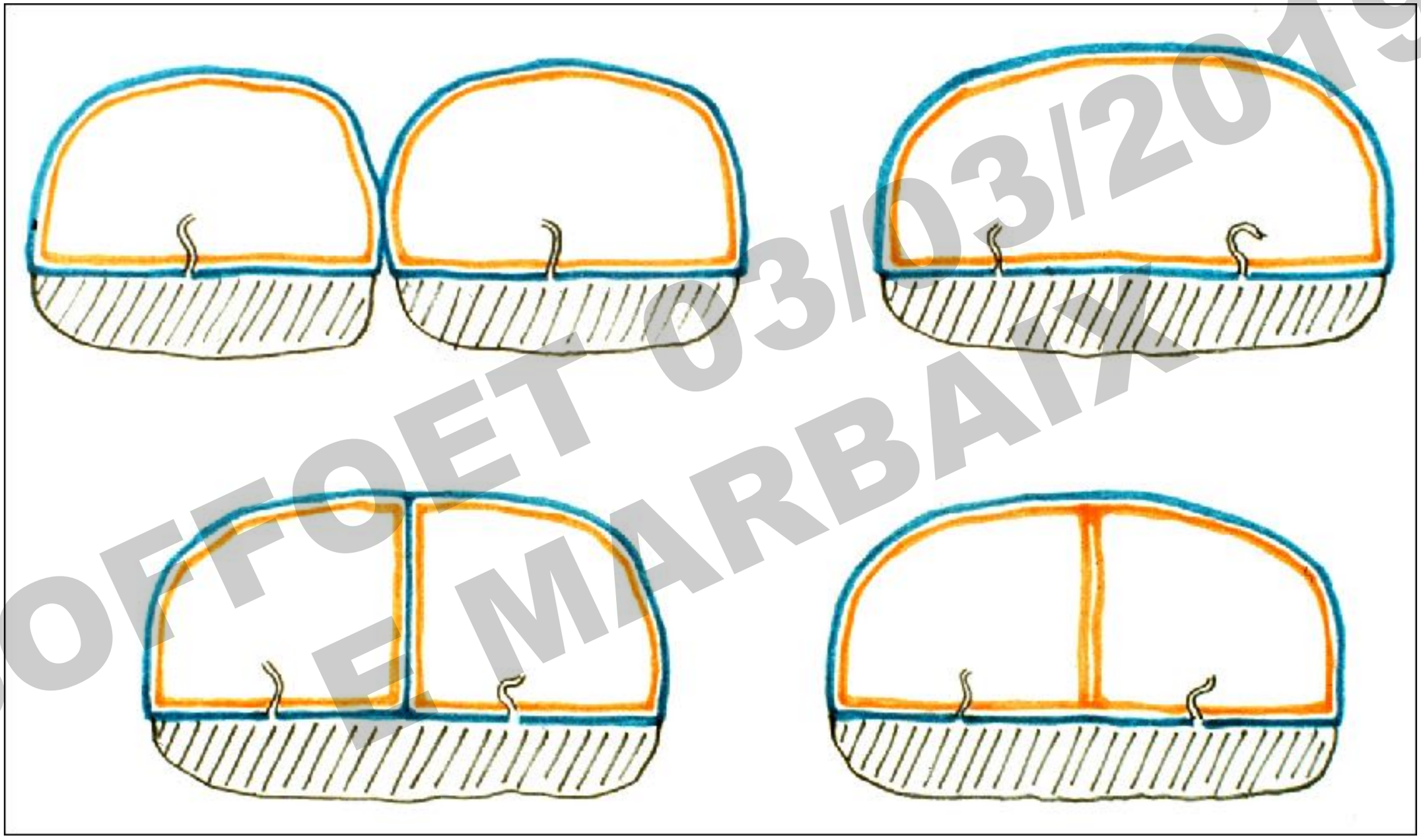
Twin pregnancies

dichorionic diamniotic monochorionic monoamniotic

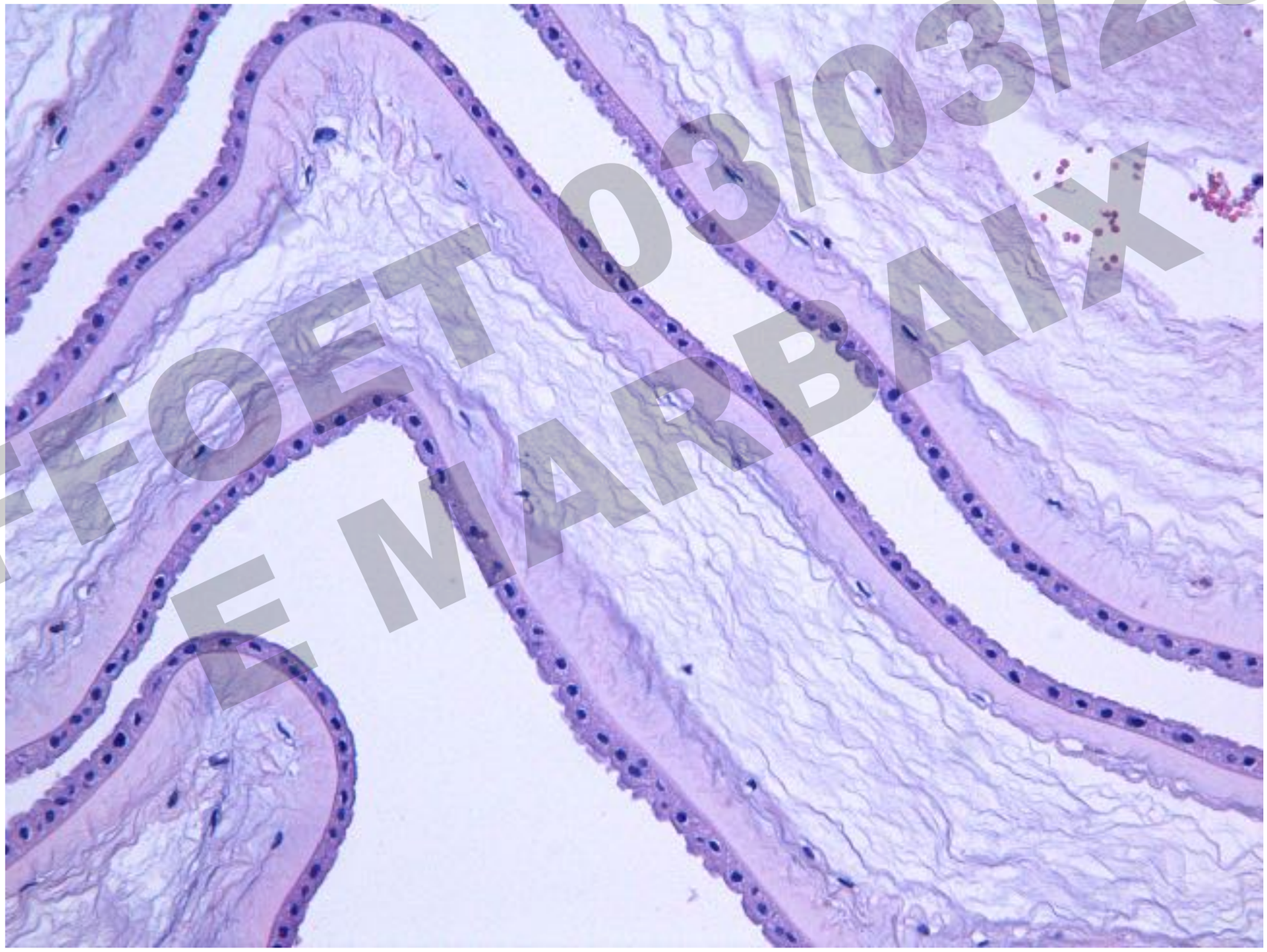


dichorionic diamniotic monochorionic diamniotic

Dichorionic diamniotic placenta

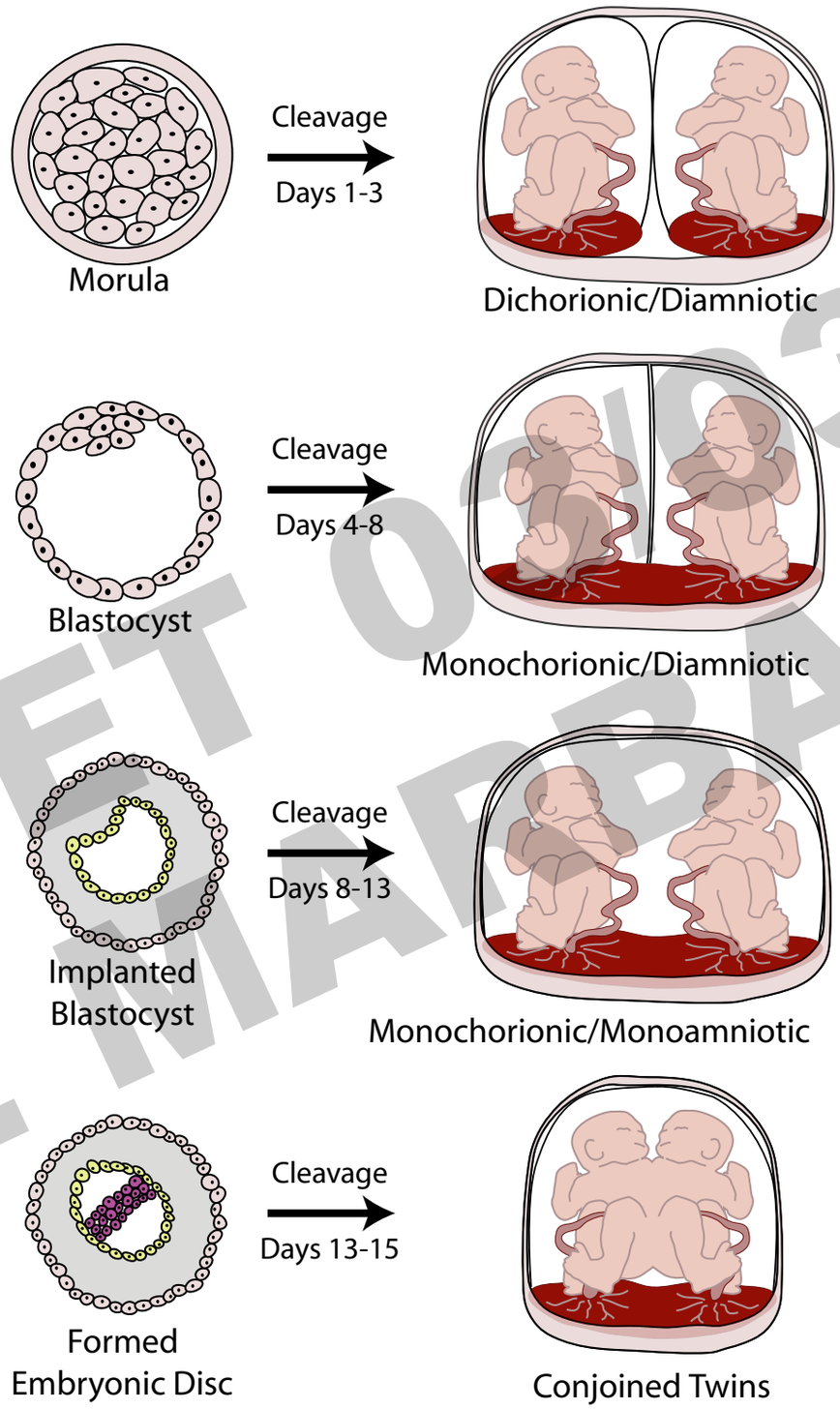
Monochorionic diamniotic placenta

Inter-twin membranes of monochorionic diamniotic placenta



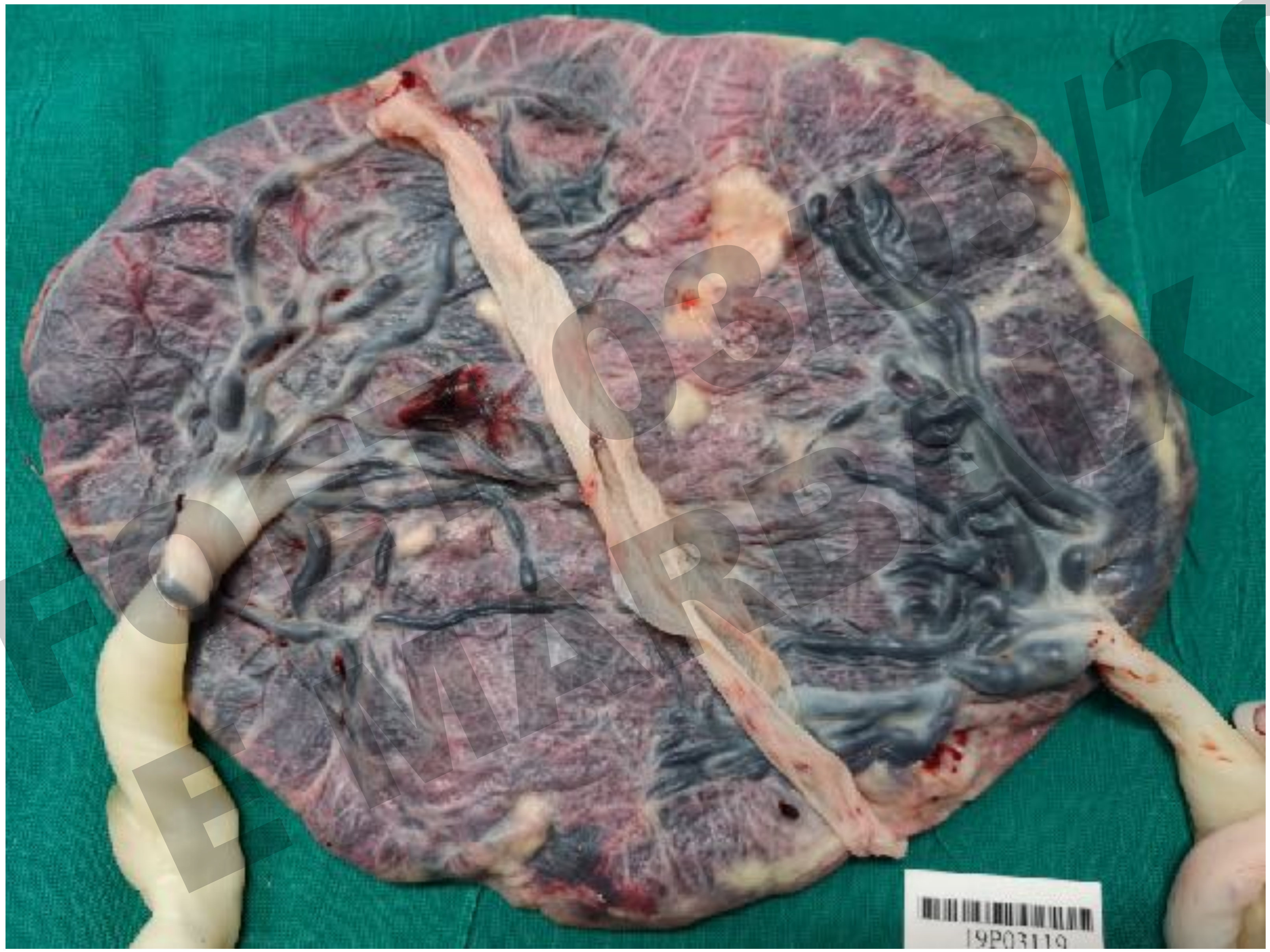
Courtesy of Dr. K. Delbecque, CHR Citadelle, Liège, Belgique

Placenta of monozygous twins



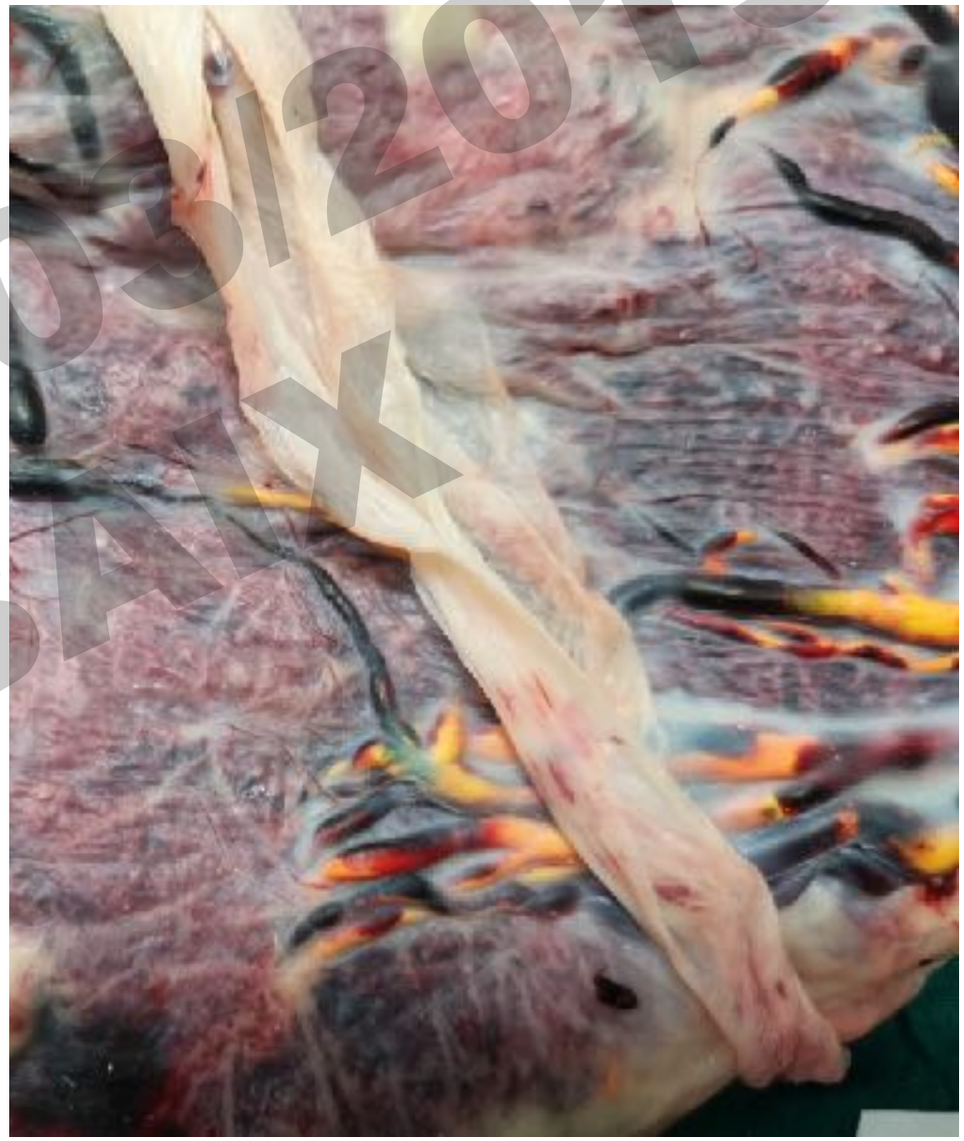
Demonstration of vascular anastomosis

Monochorionic diamniotic placenta



Courtesy of Dr. K. Delbecque, CHR Citadelle, Liège, Belgique

Demonstration of vascular anastomosis



Courtesy of Dr. K. Delbecque, CHR Citadelle, Liège, Belgique

Placental vascular anastomosis

- Monochorionic placenta: >90% anastomoses
- Arterio-arterial anastomosis: >90%, superficial, bidirectional, beneficial role
- Arterio-venous anastomosis: >90%, deep, unidirectional, deleterious role (IUGR, TAPS, TTTS)
- Veno-venous anastomosis: 25%, superficial, bidirectional, controversial role
- Dichorionic placenta: very rare but not impossible

Int J Gynecol Pathol. 2003 Oct;22(4):359-61.

Vascular anastomoses in dichorionic diamniotic-fused placentas.

Foschini MP1, Gabrielli L, Dorji T, Kos M, Lazzarotto T, Lanari M, Landini MP.
Author information

Abstract
A case of fetal twin-to-twin cytomegalovirus infection through a dichorionic diamniotic (DiDi)-fused placenta prompted our search for possible vascular anastomoses in this type of placenta. This case and three additional DiDi-fused placentas were studied with gross (macro) sections and a three-dimensional (3D) stereomicroscopic technique. Two twins were dizygotic (they differed in gender and blood groups) and the other two were probably monozygotic. Macrosections and 3D-image analysis demonstrated side-to-side connections between small subchorionic vessels. These findings demonstrate that vascular anastomoses are present in DiDi-fused placentas.

Placenta. 1989 Jan-Feb;10(1):55-9.

Vascular anastomoses in fused, dichorionic twin placentas resulting in twin transfusion syndrome.

Lage JM1, Vanmarter LJ, Mikhail E.
Author information

Abstract
We have provided pathologic documentation of vascular anastomoses across fused, dichorionic placentas. These placental anastomoses resulted in the twin transfusion syndrome.

Germ-line chimerism and paternal care in marmosets (*Callithrix kuhlii*)

C. N. Ross*†, J. A. French‡, and G. Ortí*

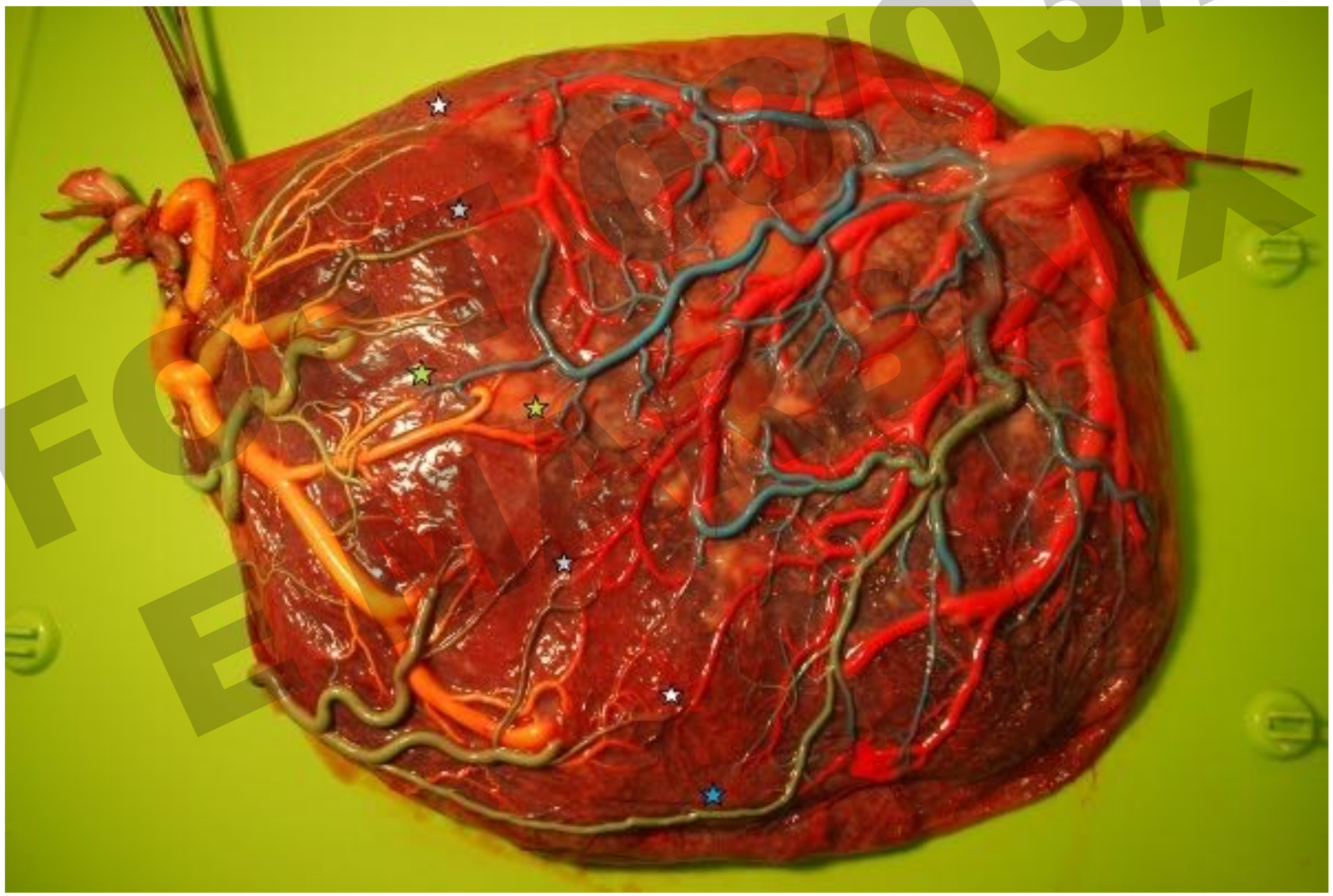
6278–6282 | PNAS | April 10, 2007 | vol. 104 | no. 15

Edited by John C. Avise, University of California, Irvine, CA, and approved Februa

The formation of viable genetic chimeras in mammals through the transfer of cells between siblings *in utero* is rare. Using microsatellite DNA markers, we show here that chimerism in marmoset (*Callithrix kuhlii*) twins is not limited to blood-derived hematopoietic tissues as was previously described. All somatic tissue types sampled were found to be chimeric. Notably, chimerism was demonstrated to be present in germ-line tissues, an event never before documented as naturally occurring in a primate. In fact, we found that chimeric marmosets often transmit sibling alleles acquired *in utero* to their own offspring. Thus, an individual that contributes gametes to an offspring is not necessarily the genetic parent of that offspring. The presence of somatic and germ-line chimerism may have influenced the evolution of the extensive

Genetic chimerism, the mingling of two or more genomic lineages within an individual (1), is rare in mammals, but chimerism is prevalent in the hematopoietic tissues of marmosets and other callitrichid primates (2, 3). In these species, fraternal twins exchange cell lines through chorionic fusion during early development (2, 4, 5). On the basis of karyotypic evidence from *Callithrix jacchus* (2, 3), estimates are that 95% of pregnancies result in the birth of hematopoietic chimeric twins. Chorionic fusion of the twins' placentas begins on day 19 and is complete by day 29, forming a single chorion with anastomoses connecting the embryos, which are still at a presomite stage in development (4–7). The fusion of the chorions and a delay in embryonic development at this stage allows the exchange of embryonic stem cells via blood flow between the twins (2, 8). As a result, the infants are genetic chimeras with tissues derived from self and sibling embryonic cell lineages (2, 3, 8).

Monochorionic placenta from a normal twin pregnancy

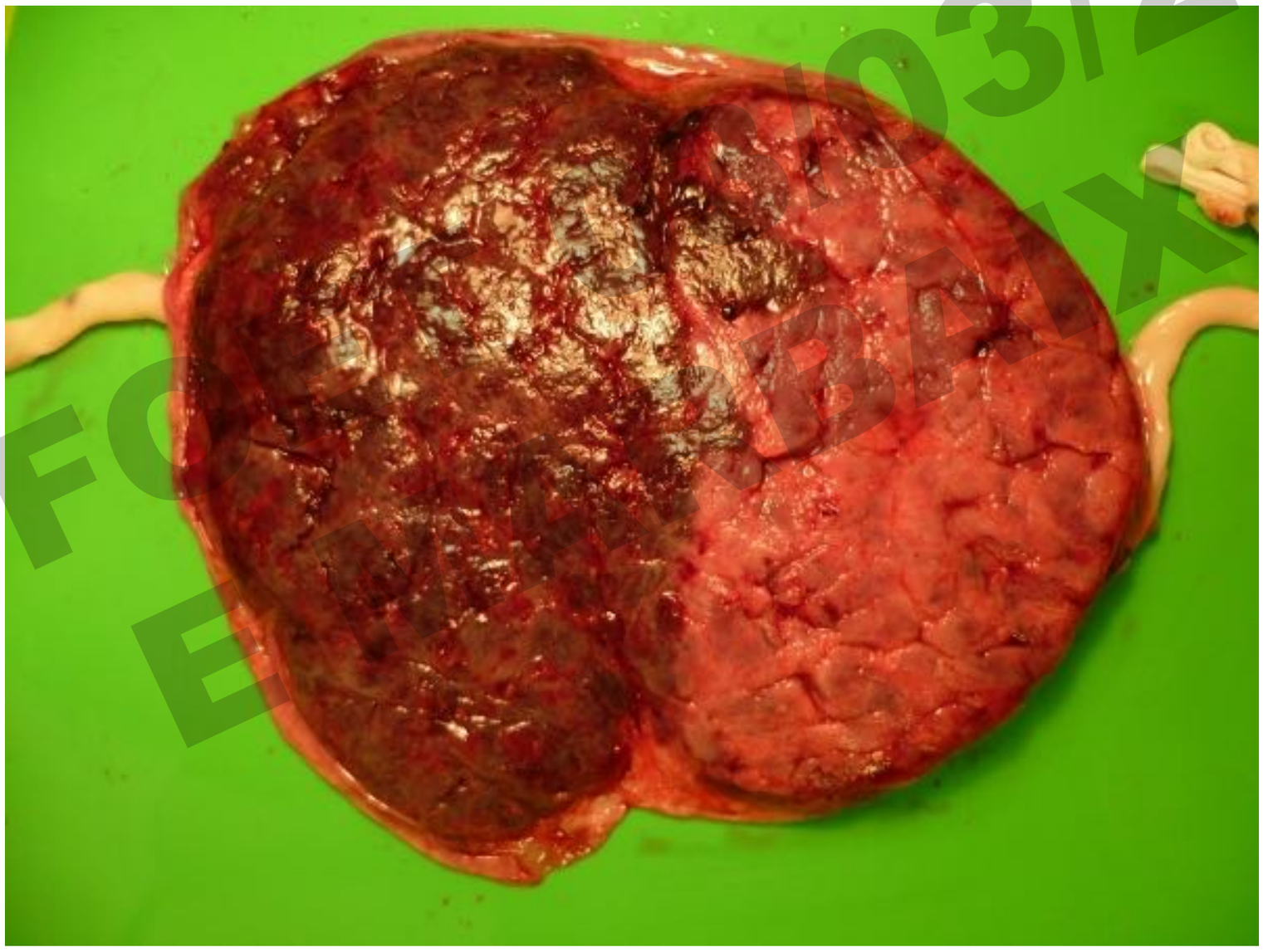


Lopriore et al, J Vis Exp 55, e3208 (2011)

TTTS placenta after fetoscopic laser coagulation of anastomoses

Lopriore et al, J Vis Exp 55, e3208 (2011)

Maternal side of TAPS placenta



Lopriore et al, J Vis Exp 55, e3208 (2011)

Umbilical cord entanglement

Courtesy of Dr. K. Delbecque, CHR Citadelle, Liège, Belgique

An unusual twin pregnancy

- Ultrasound examination at 18 weeks: normal fetus and placenta with 2 distinct parts

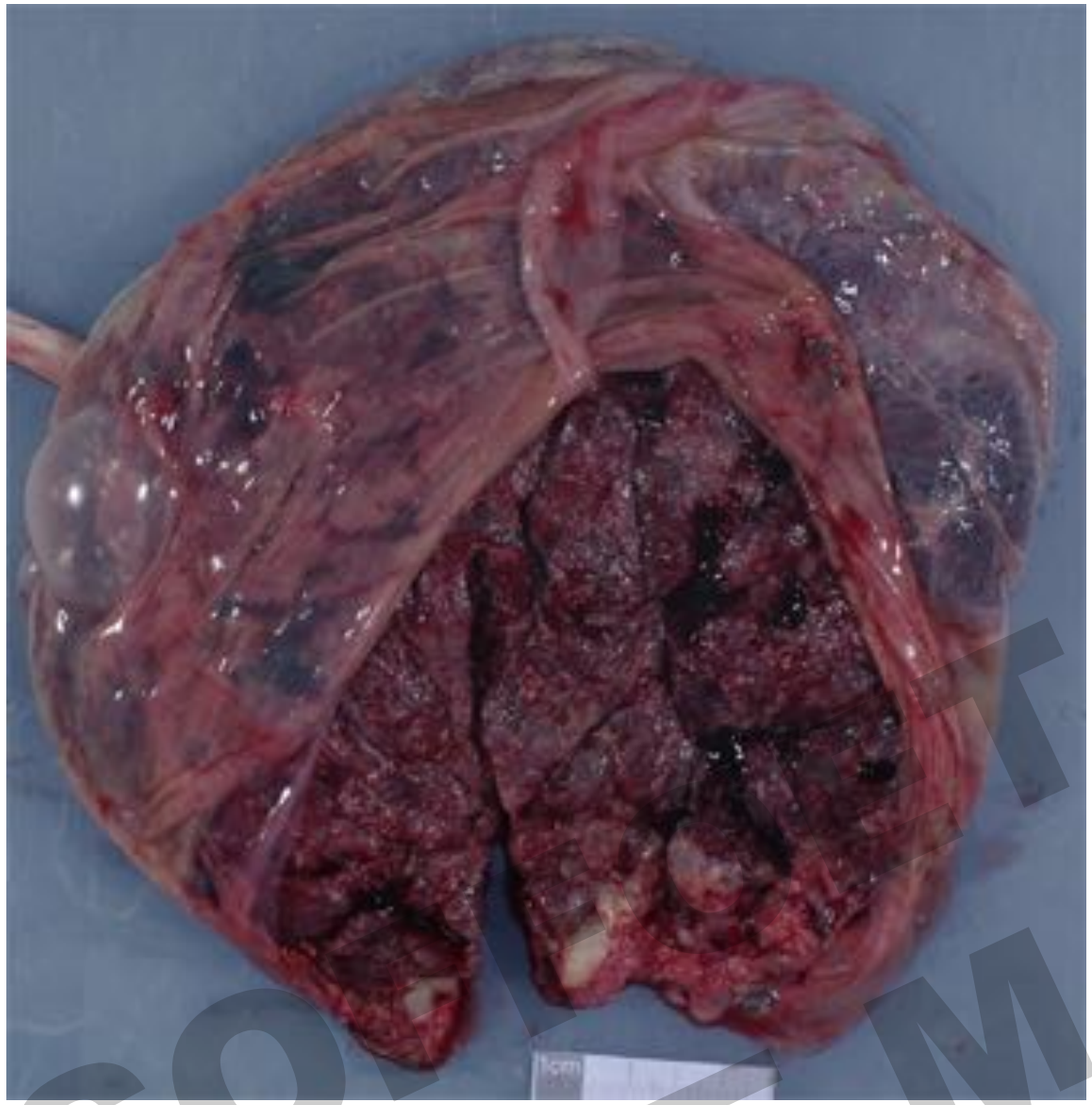
- HCG level: 175539 IU/L

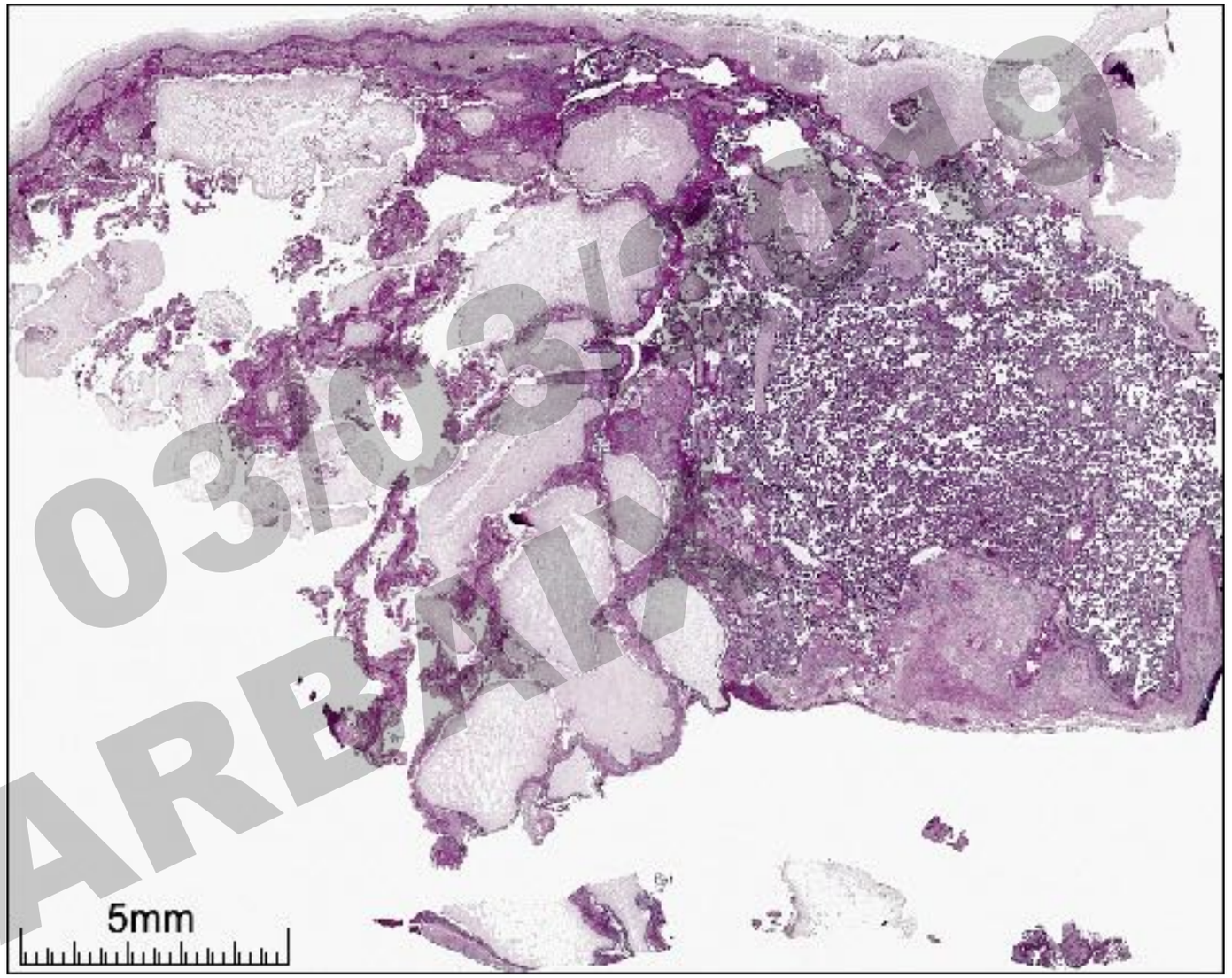
- Patient wishes to continue the pregnancy

- At 3d trimester, molar part shrinks

- At 39 weeks, spontaneous delivery of a normal 3950 g male baby

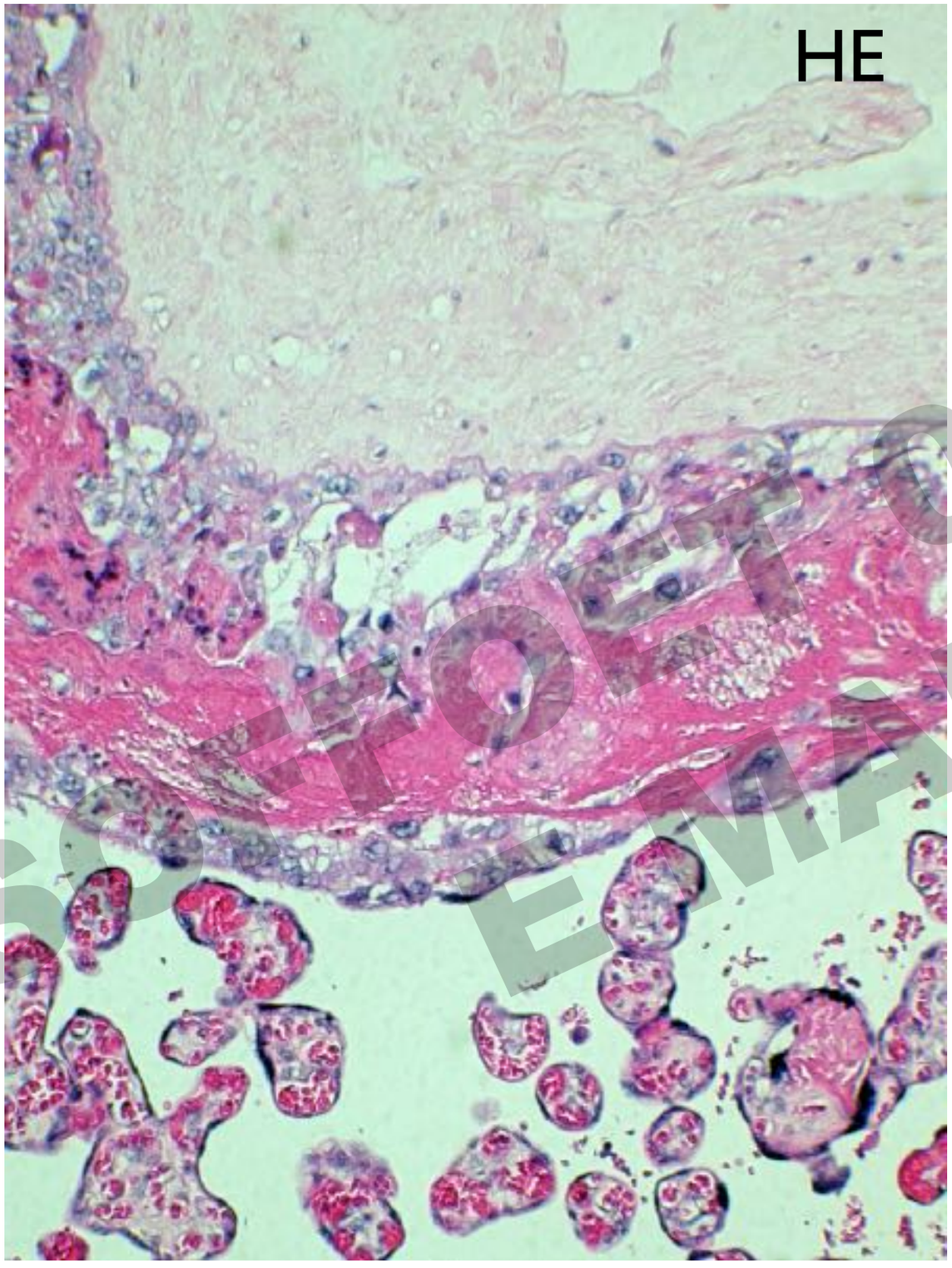
Pathological analysis of placenta

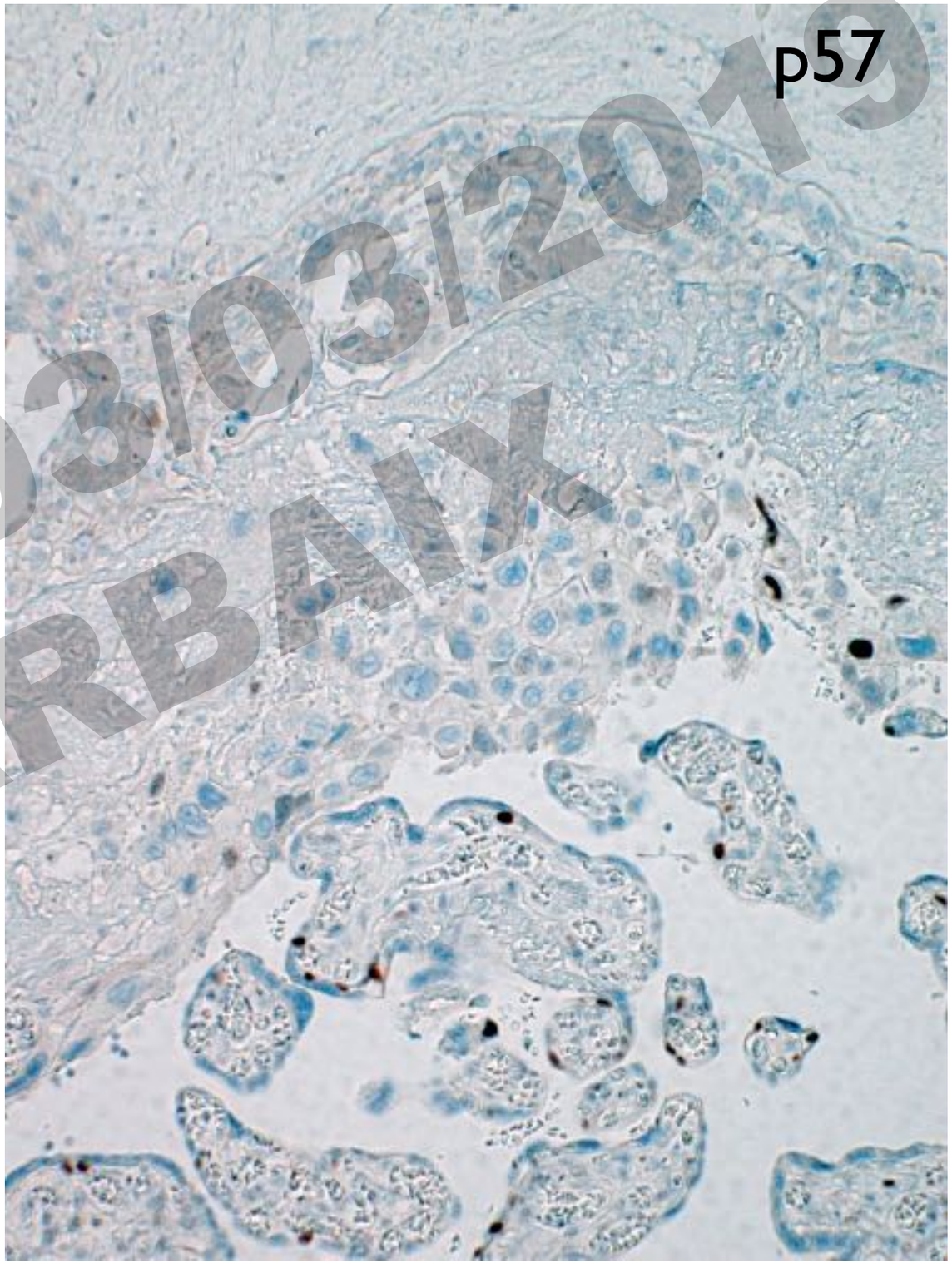




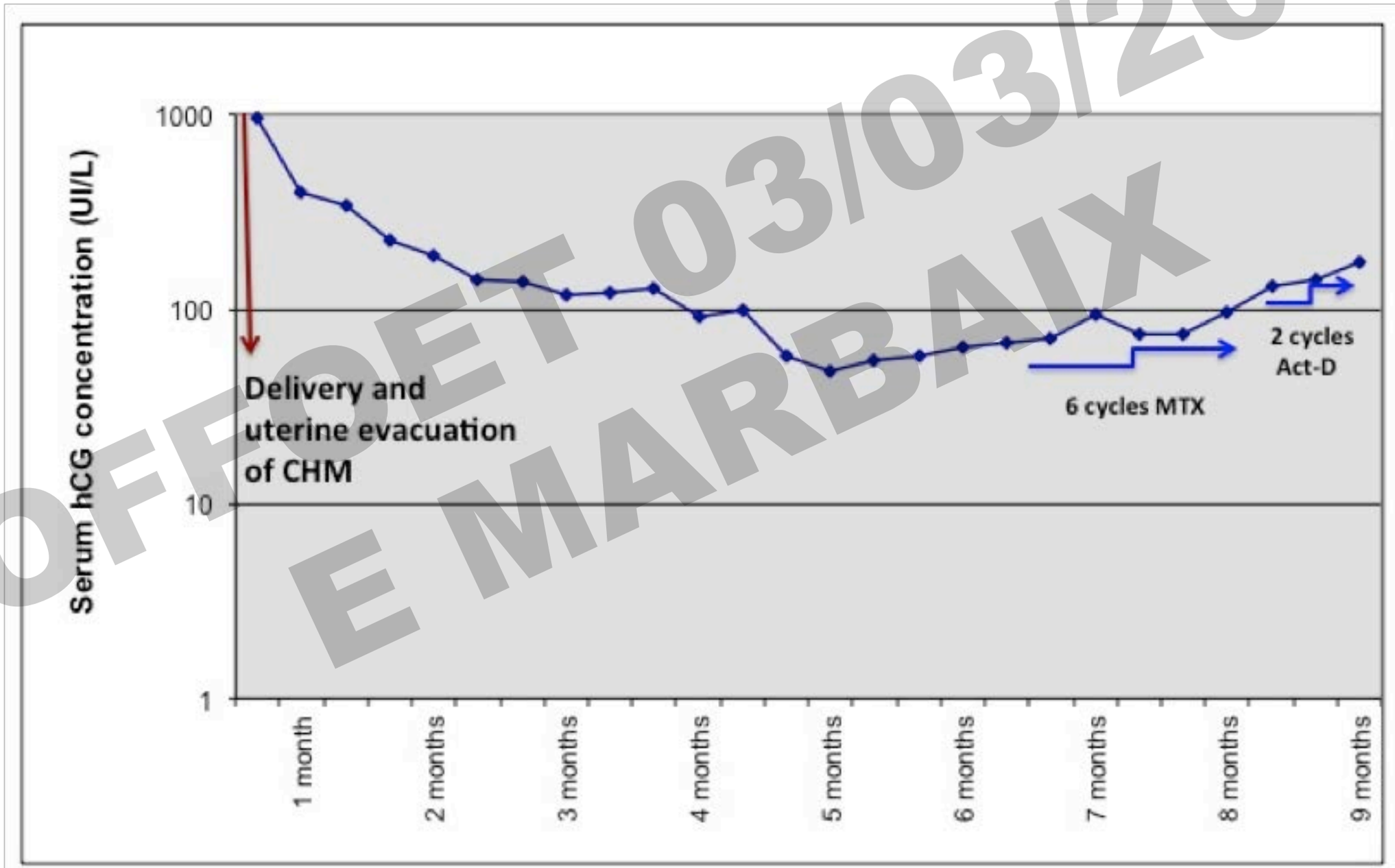
Monochorial placenta with complete hydatidiform mole and normal male co-twin

Microscopic analysis of placenta





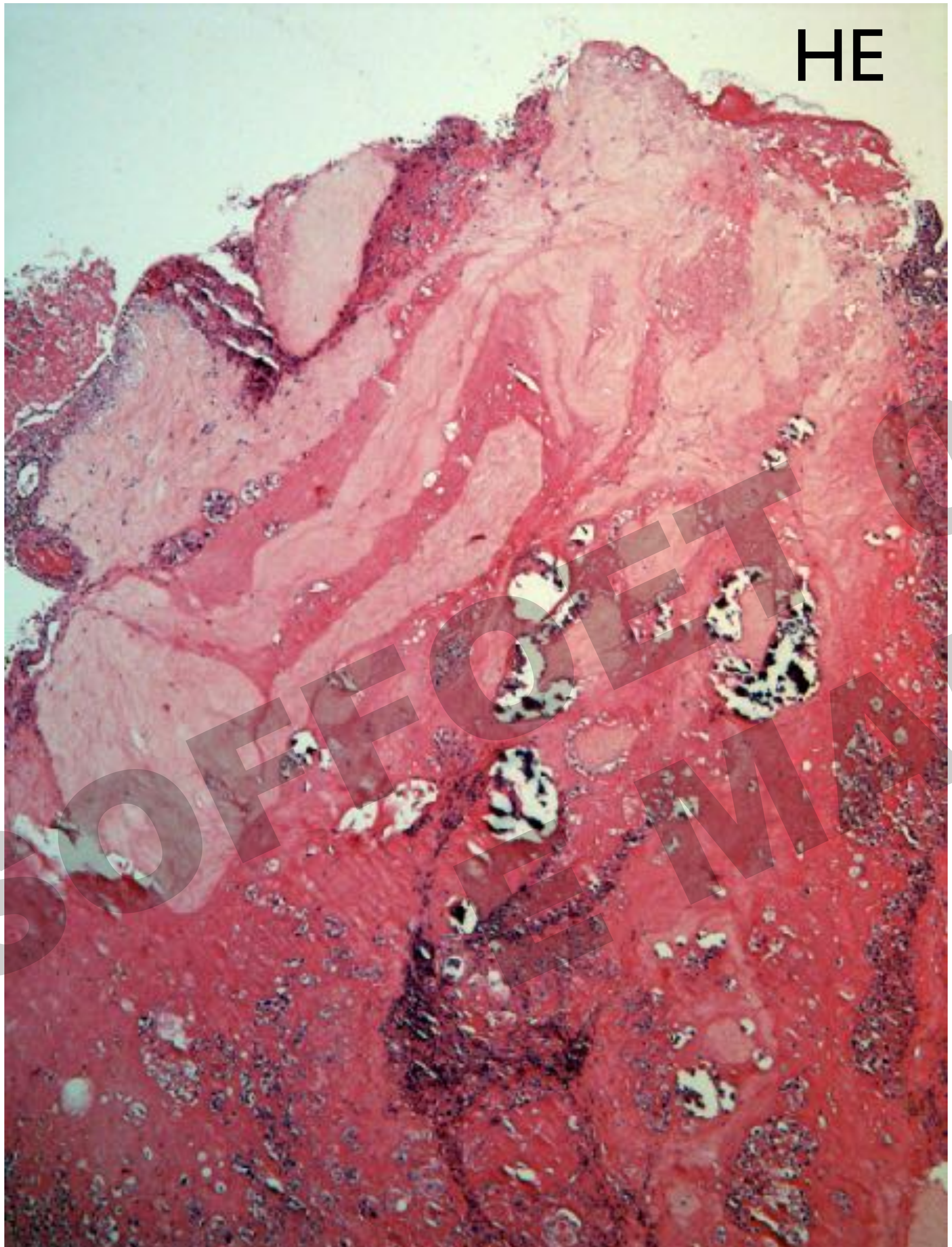
Post-partum surveillance of HCG

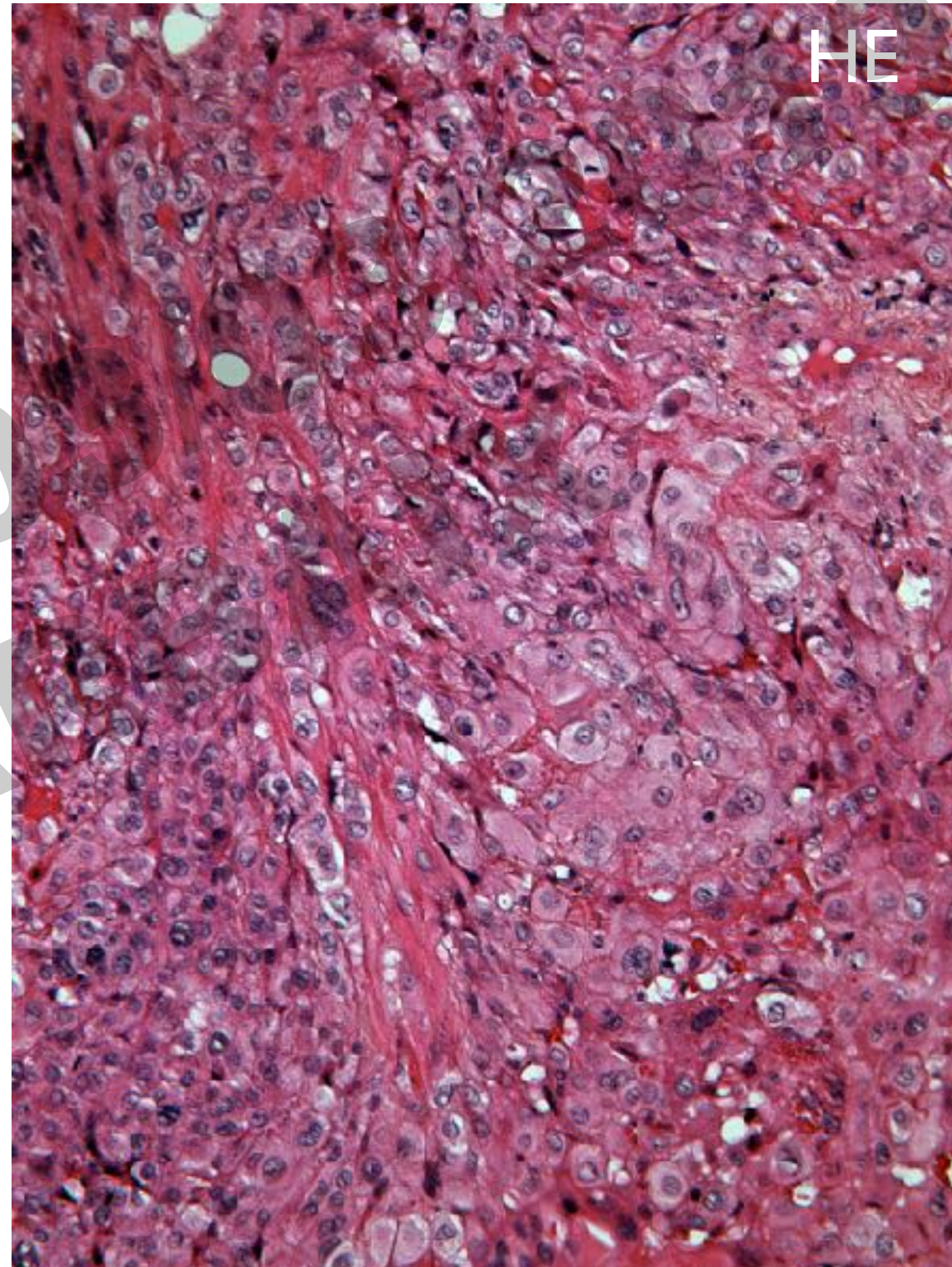


Evolution of the disease

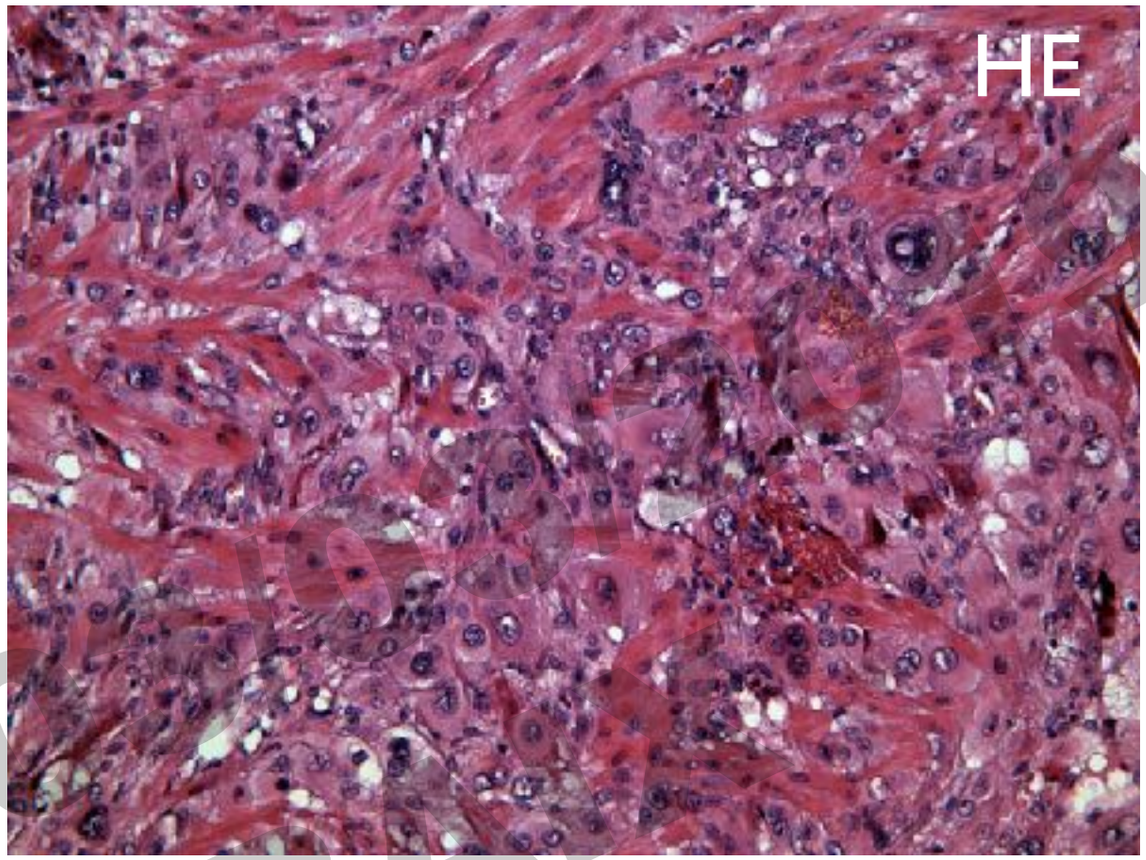
- Metrorrhagia at 10 months post-partum
- Curettage: persistence of molar villi and placental site trophoblastic tumour
- Transvaginal ultrasound: heterogeneous vascularized mass invading myometrium
- CT-scan and MRI: no pelvic involvement, no metastasis
- Hysterectomy with pelvic and lombo-aortic lymphadenectomy

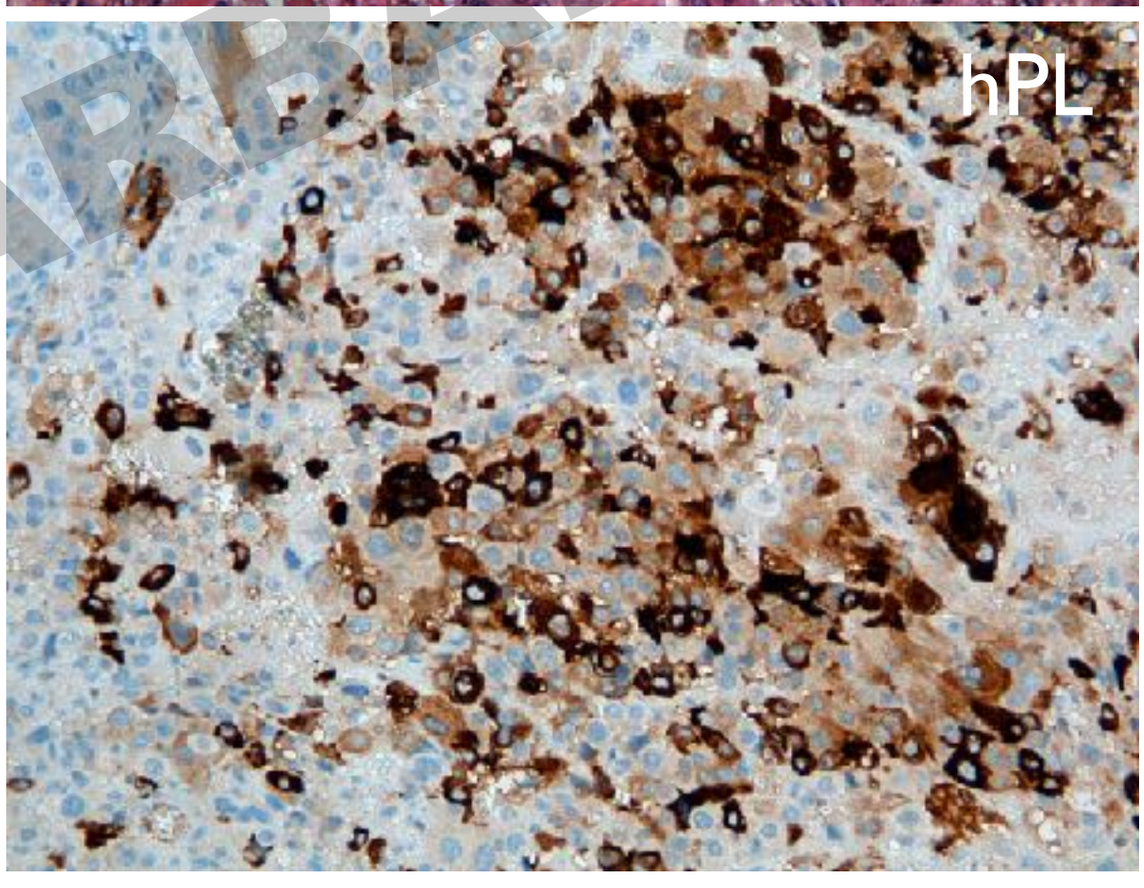
Microscopic analysis of curettage



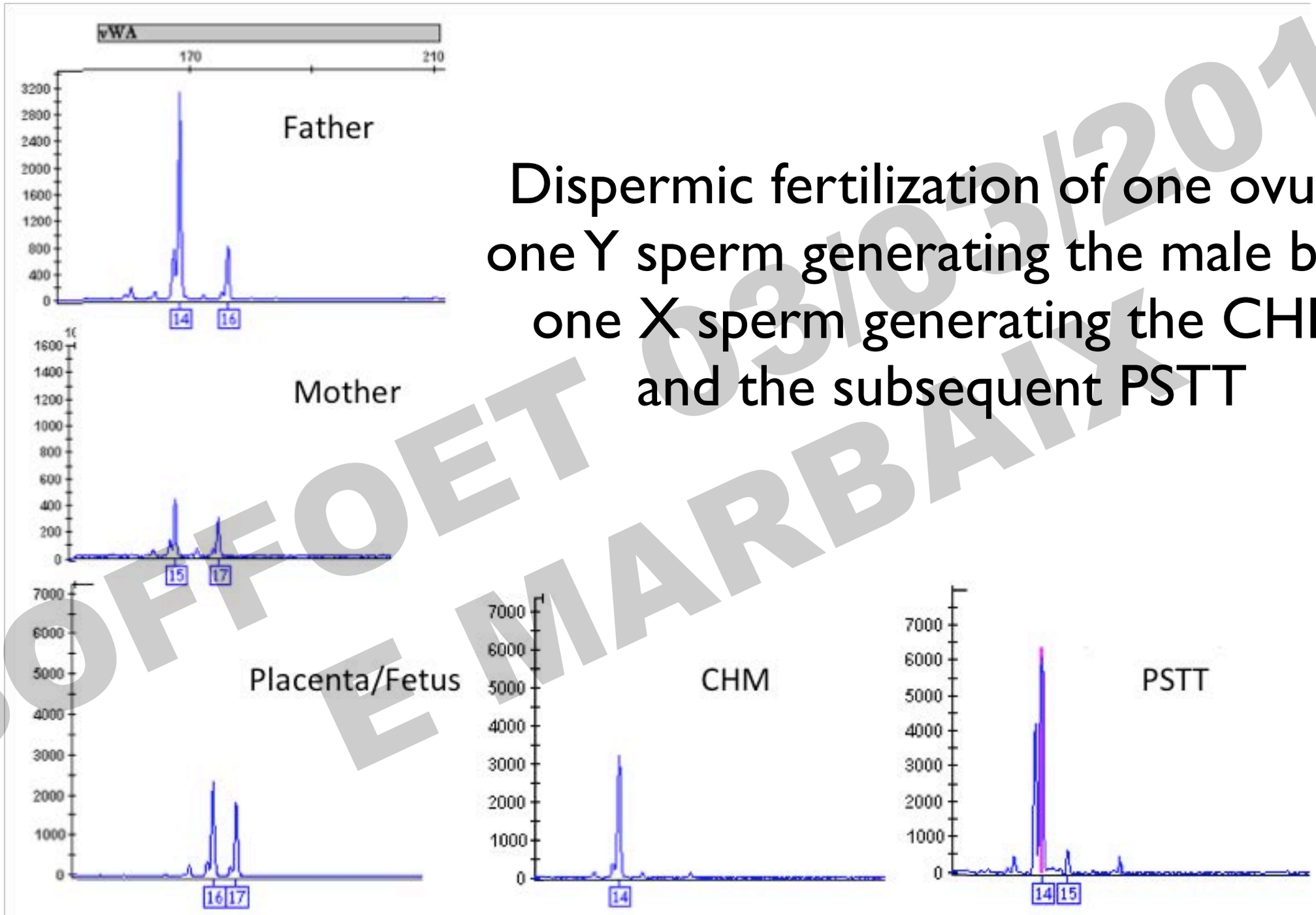


PSTT



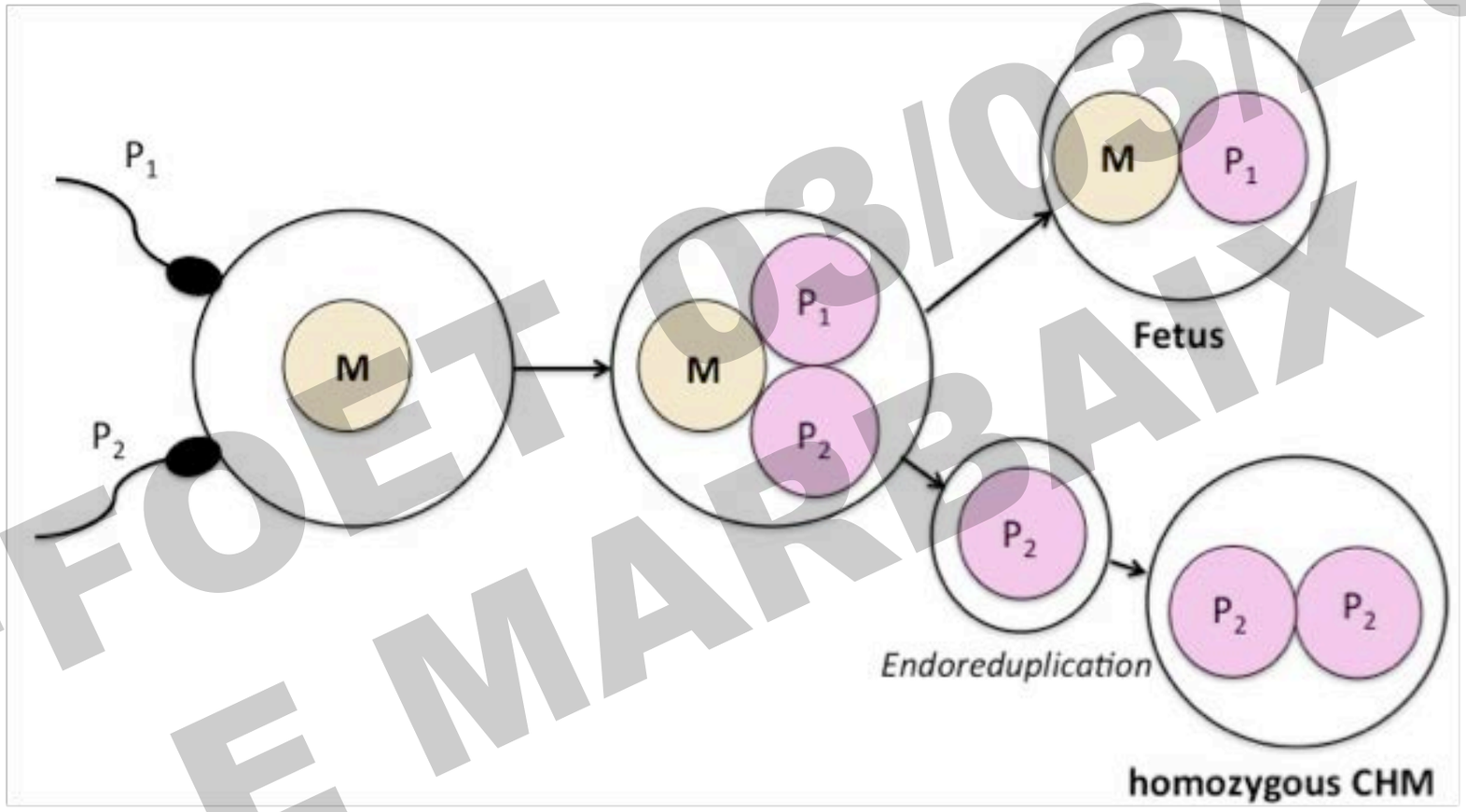


Microsatellite analysis in vWA locus



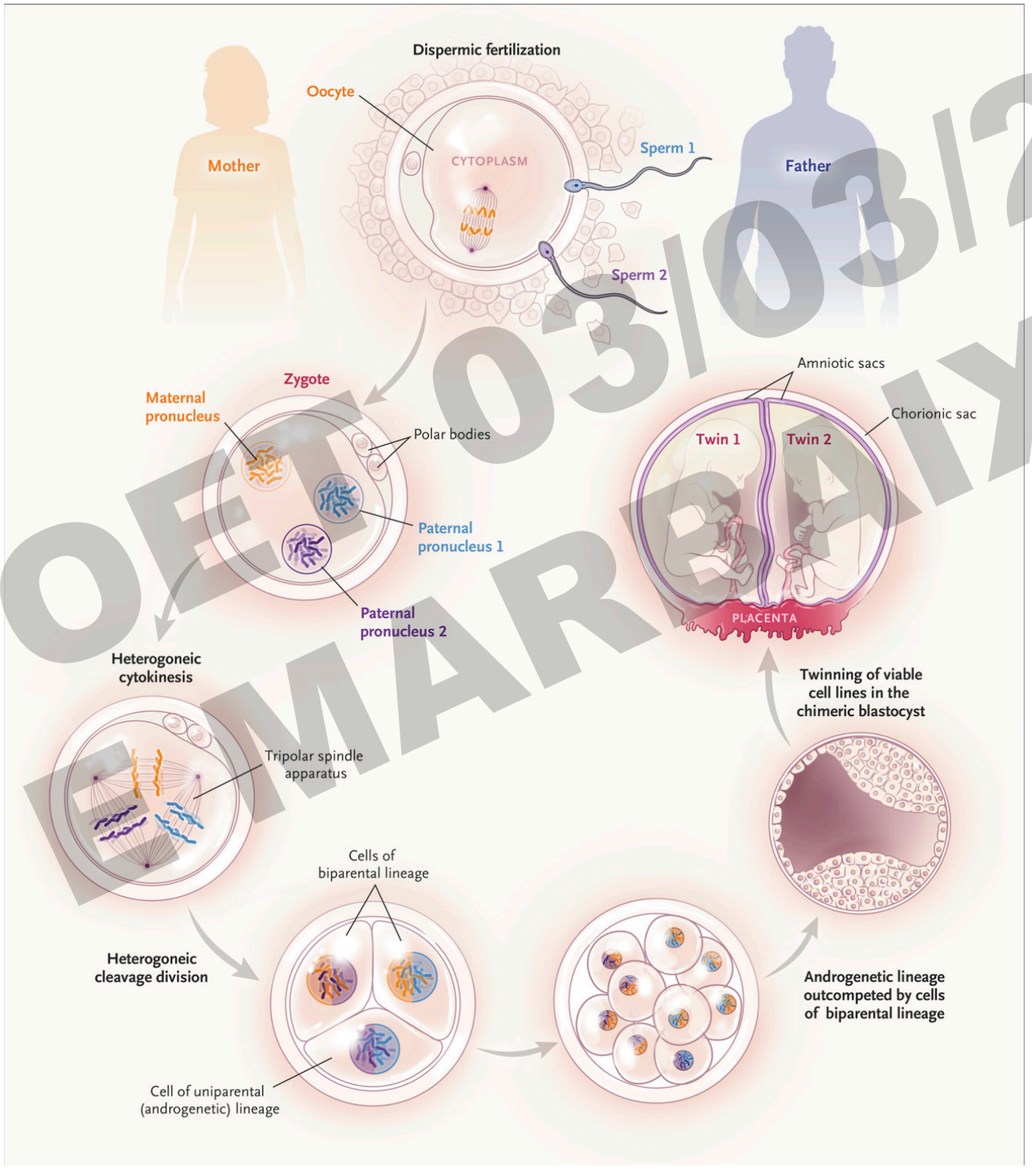
Dispermic fertilization of one ovum:
one Y sperm generating the male baby
one X sperm generating the CHM
and the subsequent PSTT

Fertilization scenario in CMCF



Hoffner & Surti, Cancer Genetics 2012

Sesquizygotic twins



Gabbett et al, New Engl J Med 2019