



IN UTERO FŒTAL DEATH AN ADDITIONAL CAUSE TO CONSIDER

*Radia FRITIH, Julia TORRENTS, Emmanuelle LESIEUR,
Sophie COLLARDEAU-FRACHON, Frederic FINA, Christine ZANDOTTI, Céline GAZIN*

Department of Pathology and Neuropathology, Timone's Hospital, Marseille, France

Journées BEST OF SOFFŒT 15/10/2021

OBSERVATON

- A 40-year-old woman, gravida 3, para 2, was admitted to the maternity emergency unit at 24⁺² WG for decreased active foetal movements
- Thrombocytopenia: 100.000 G/L
- Haemoglobin: 11.5 g/dl

Next Day: IUD

Autopsy

mild growth retardation \approx 23 WG

a



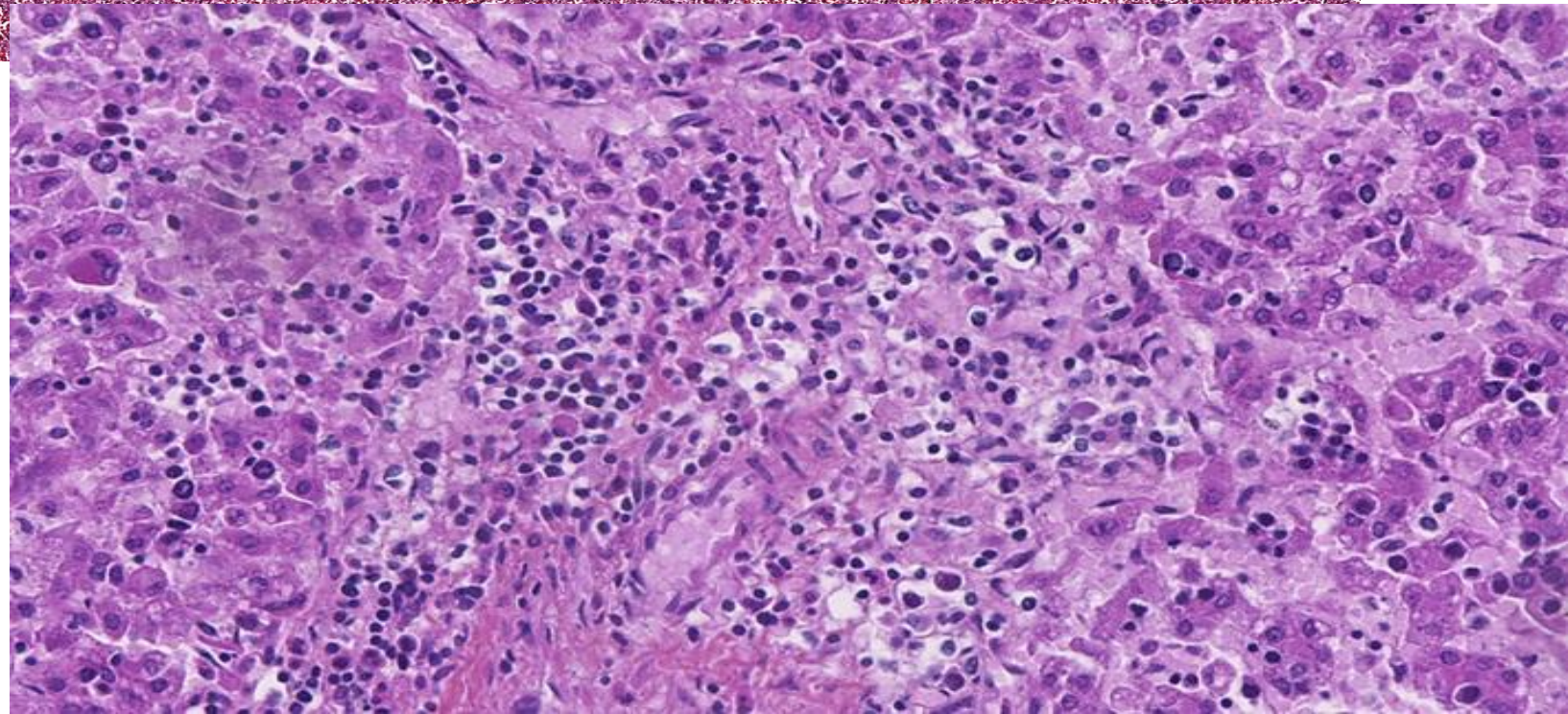
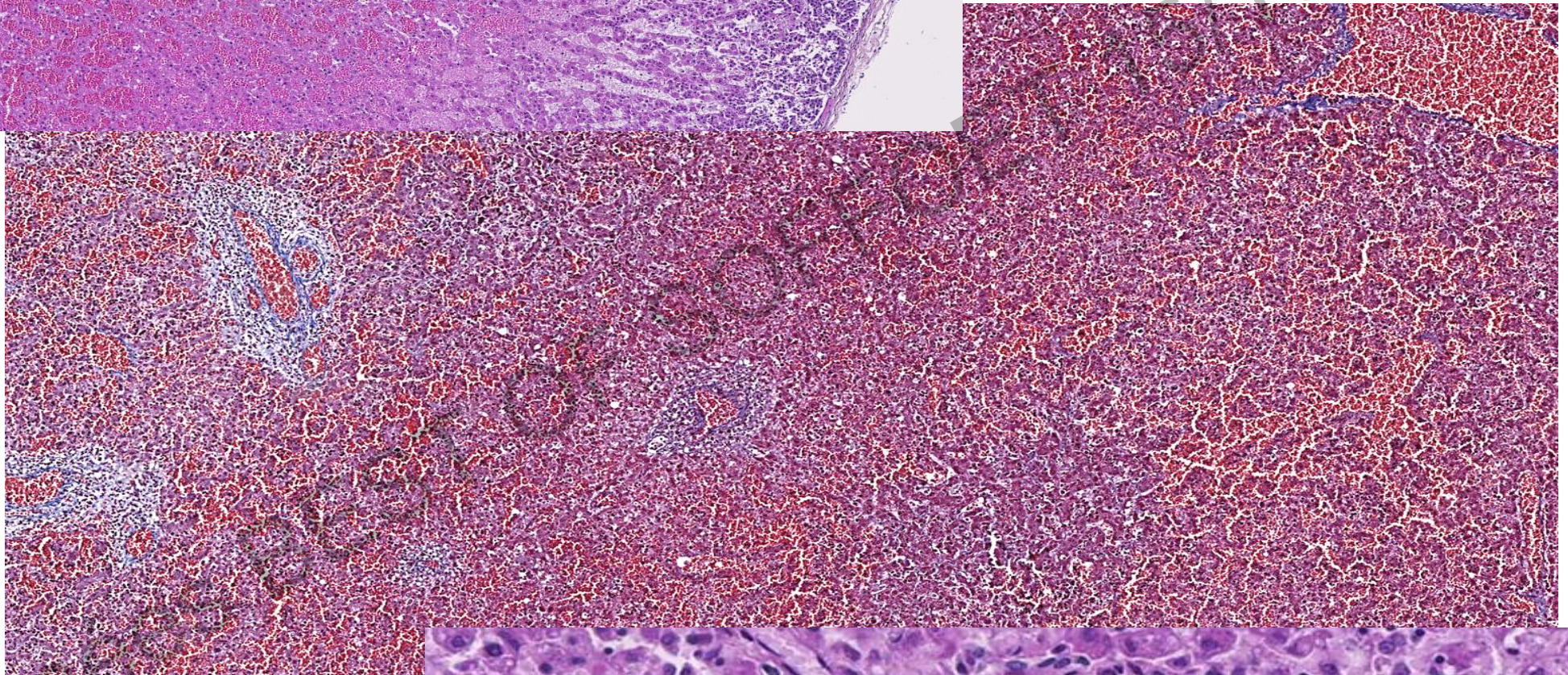
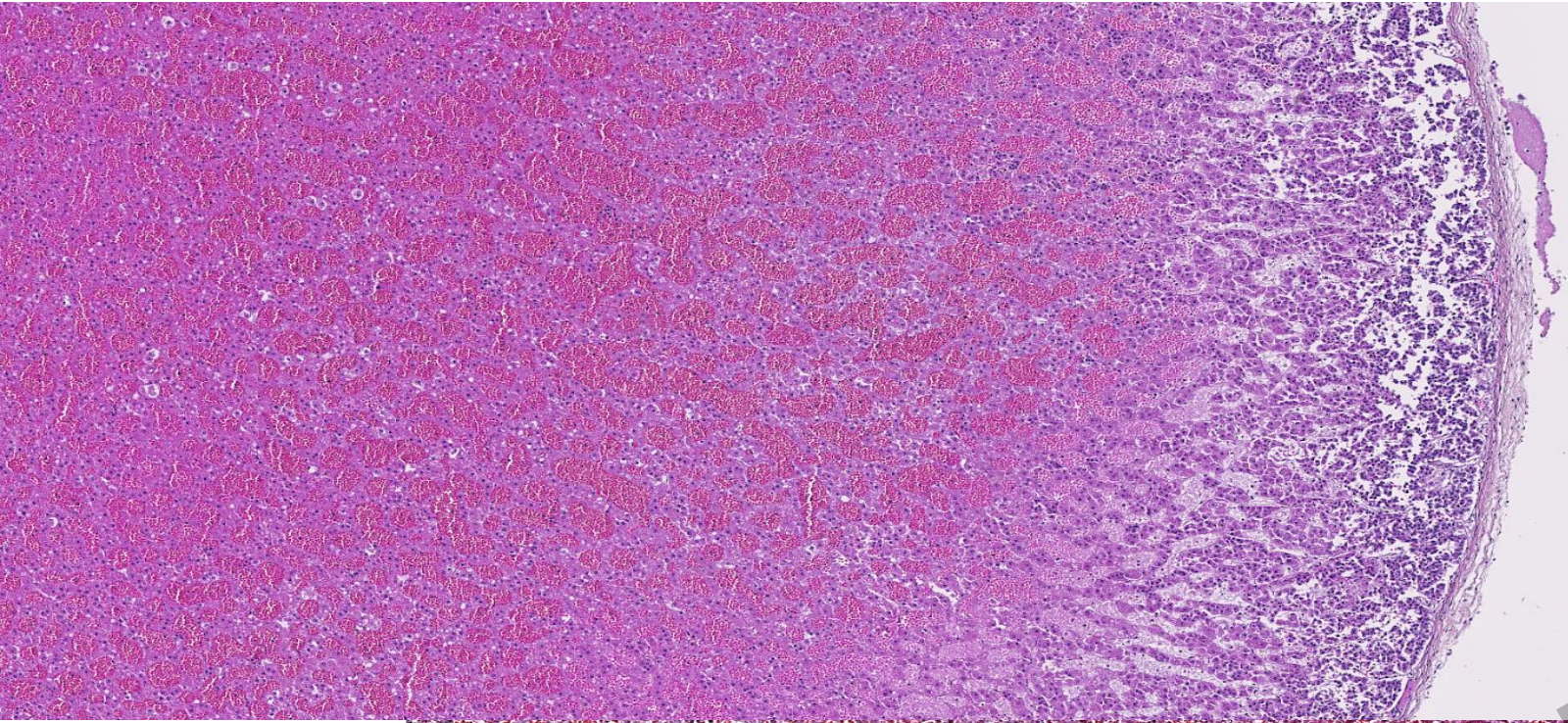
b



Macroscopic examination of fetal viscera: mild cardiomegaly with multiple petechiae (arrow) found at the level of the hepatic surface (a) and the bases of the right and left pulmonary lobes (b)

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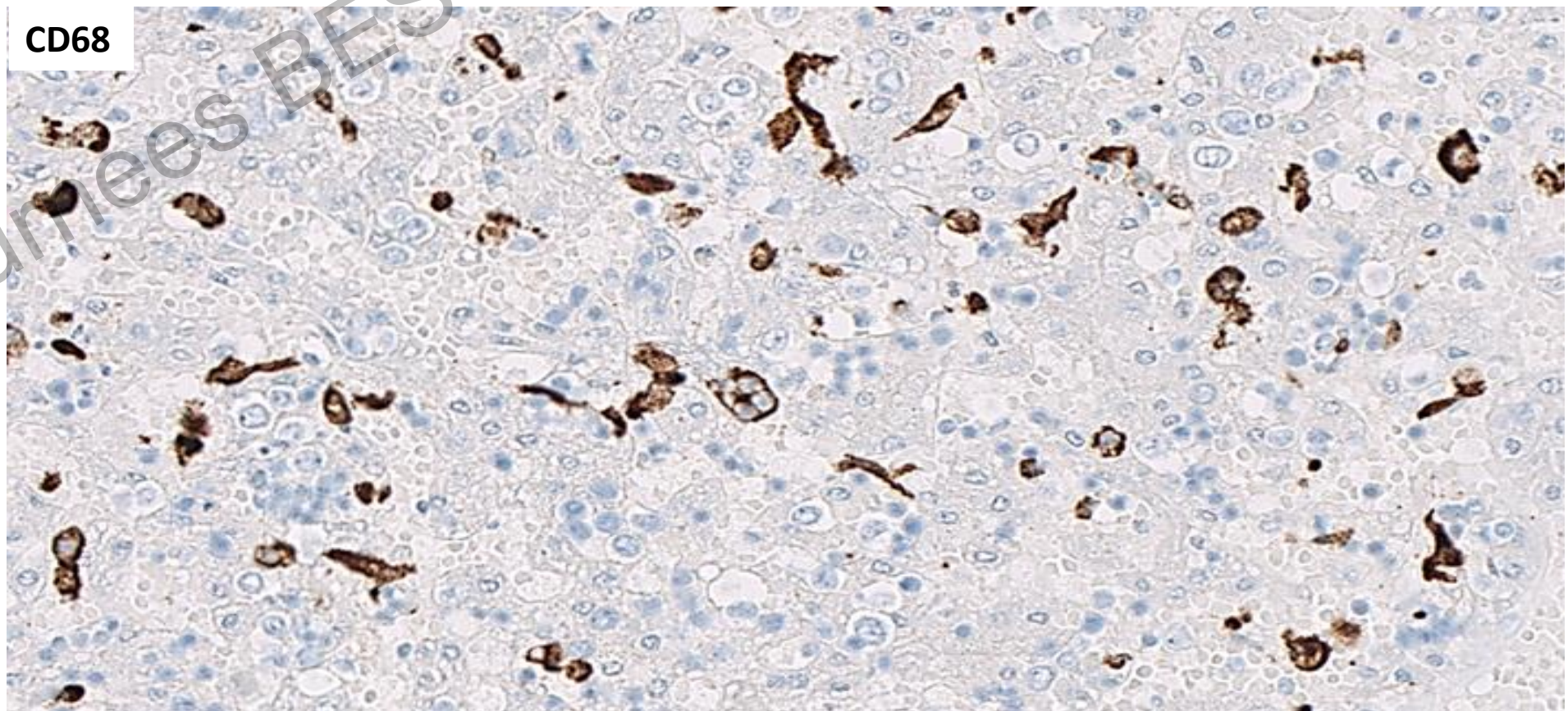
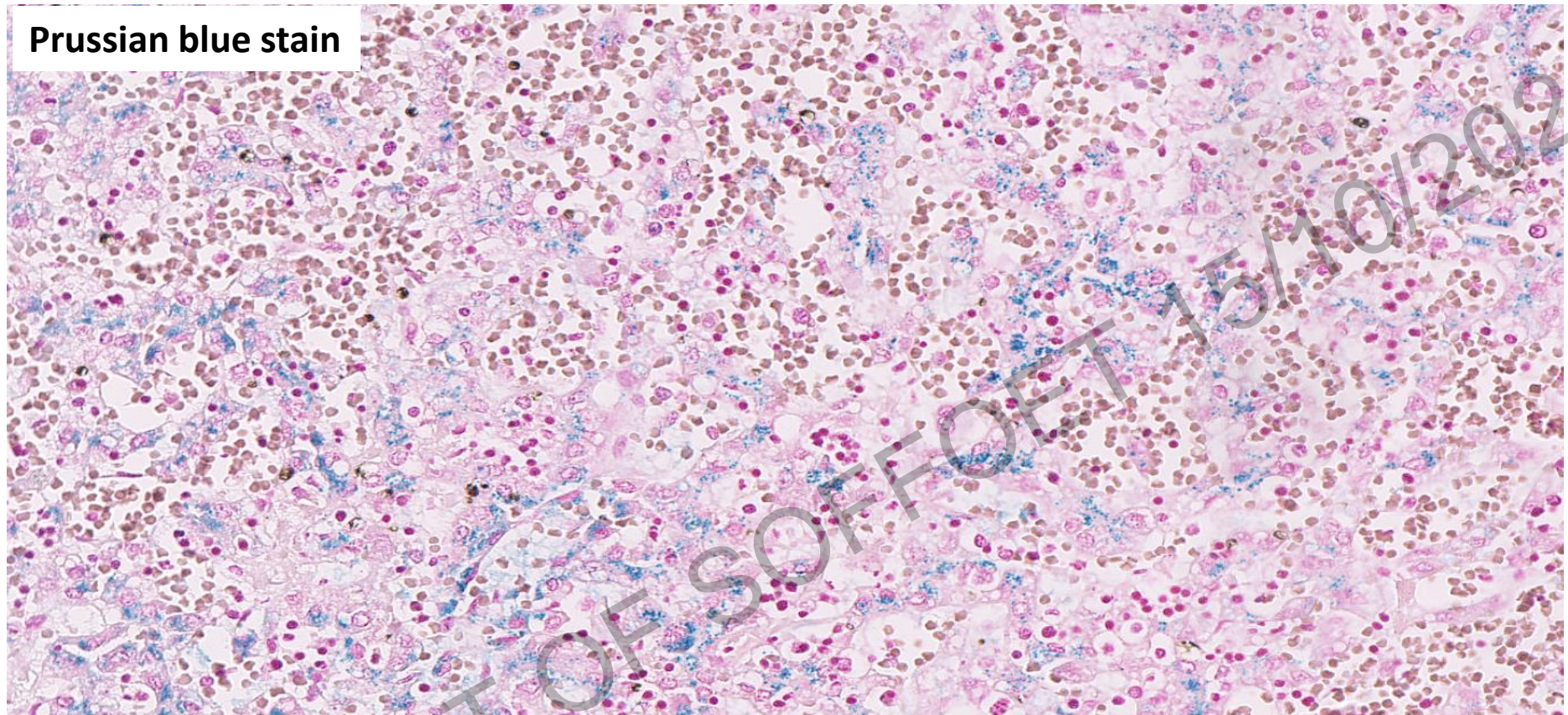
Fetal specimens



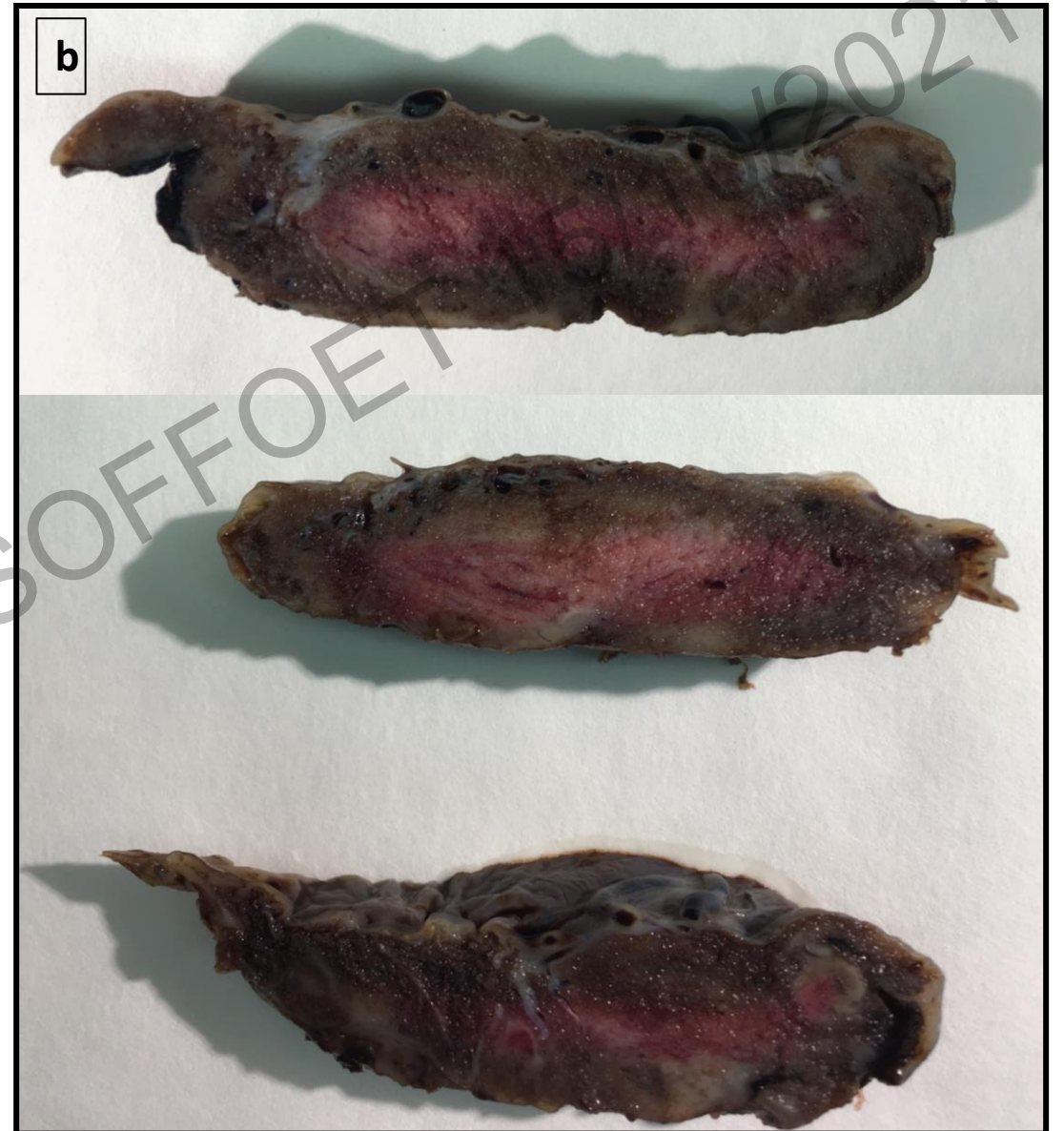
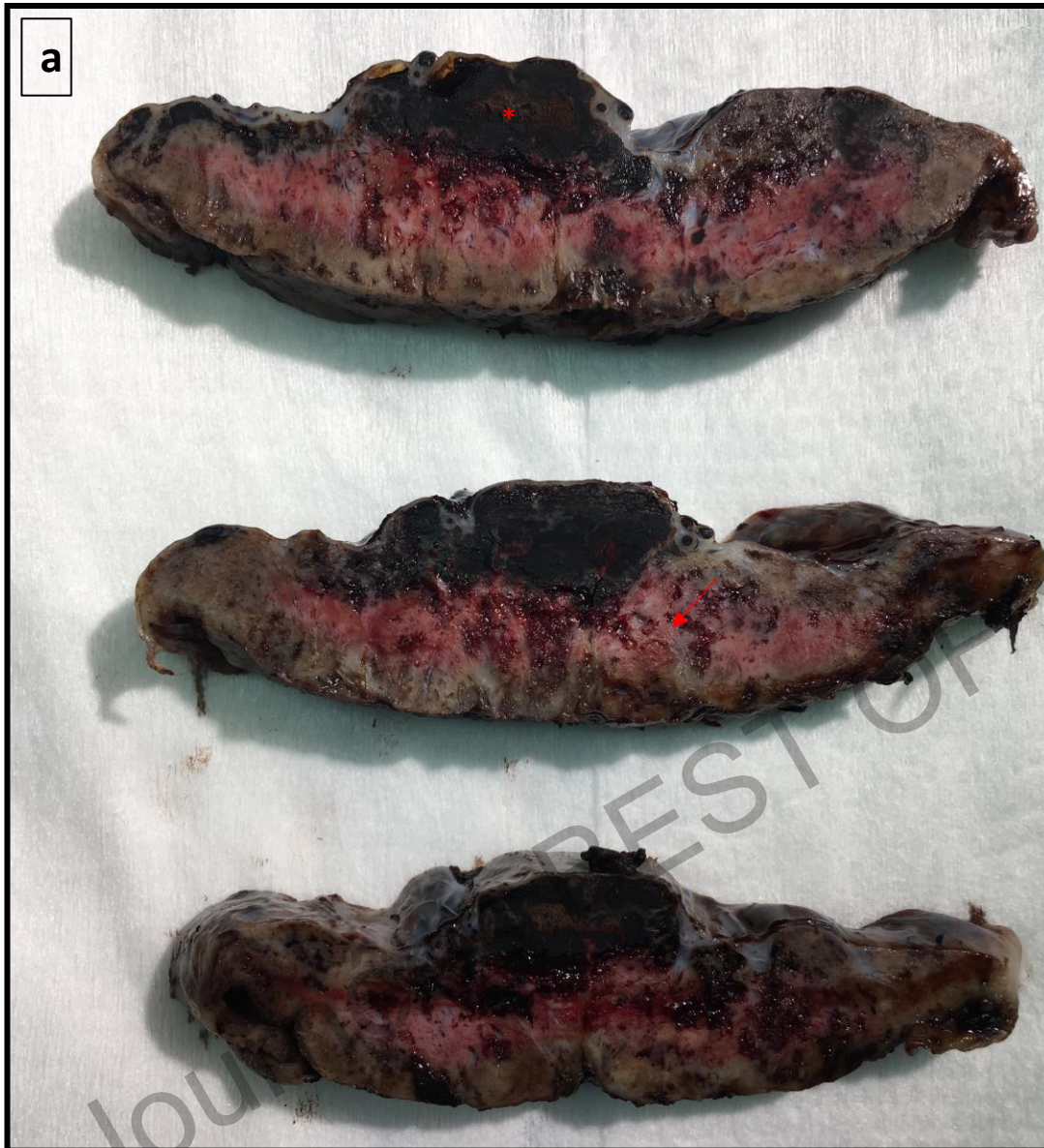
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Journe

Fetal specimens

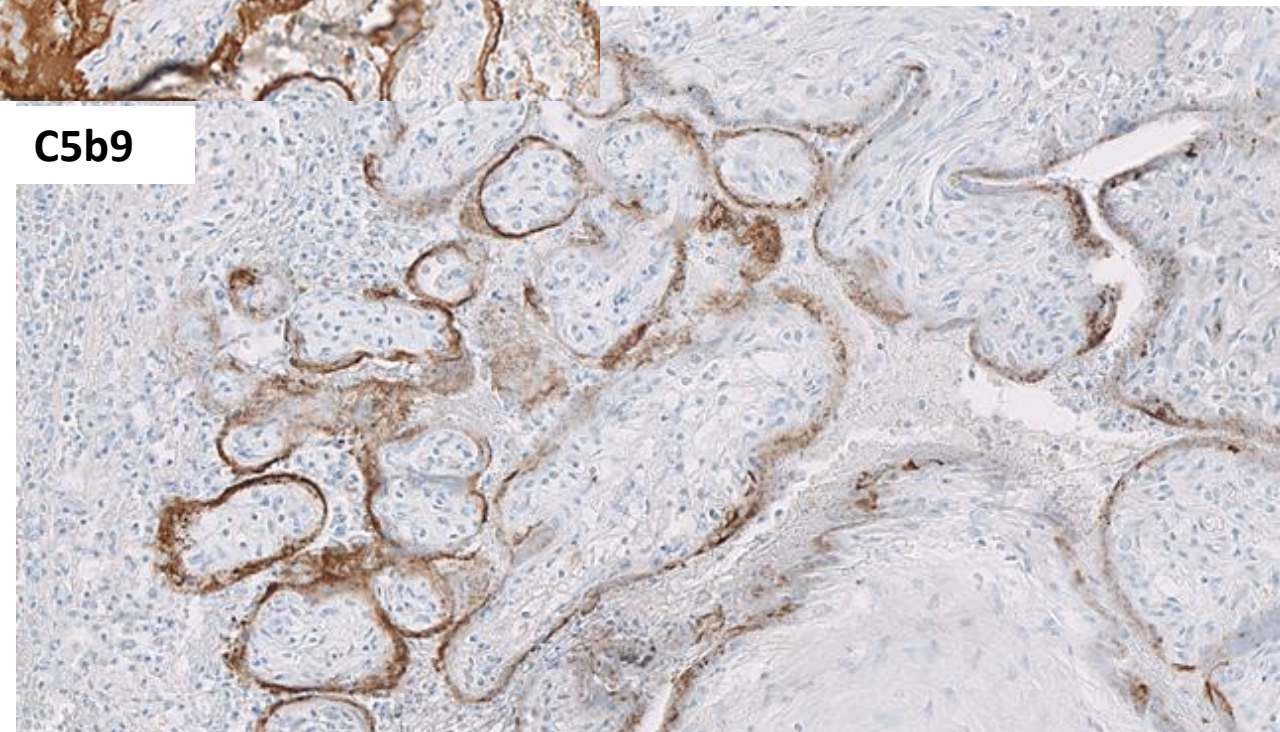
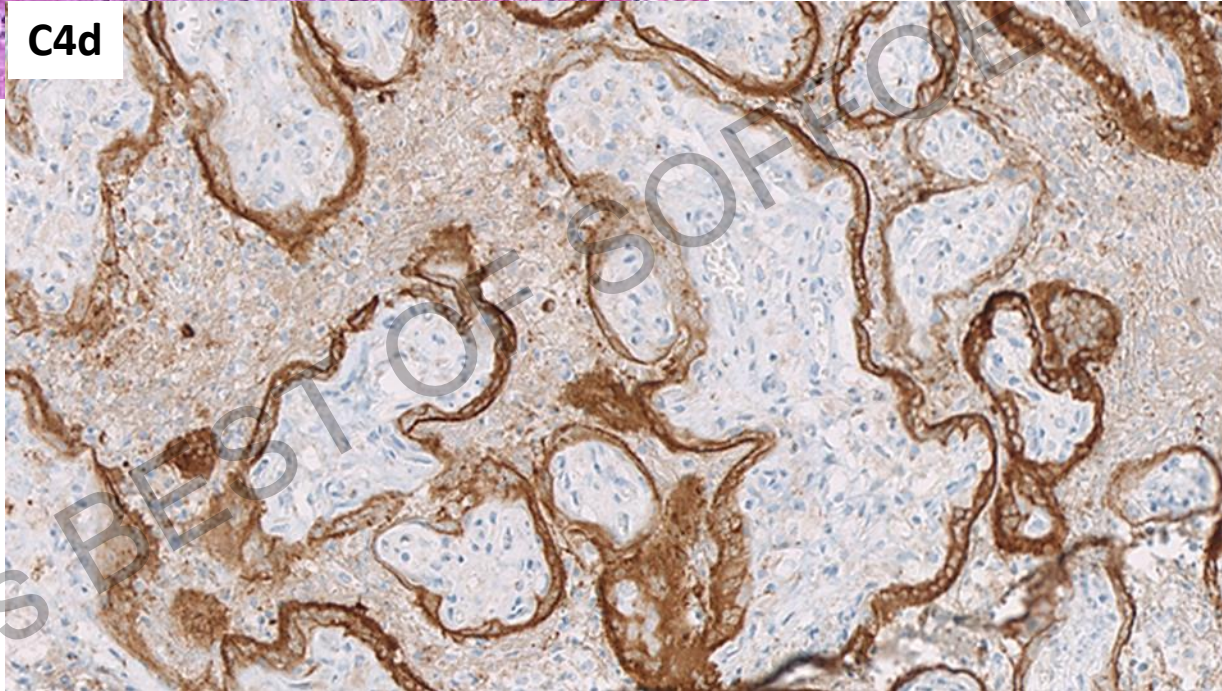
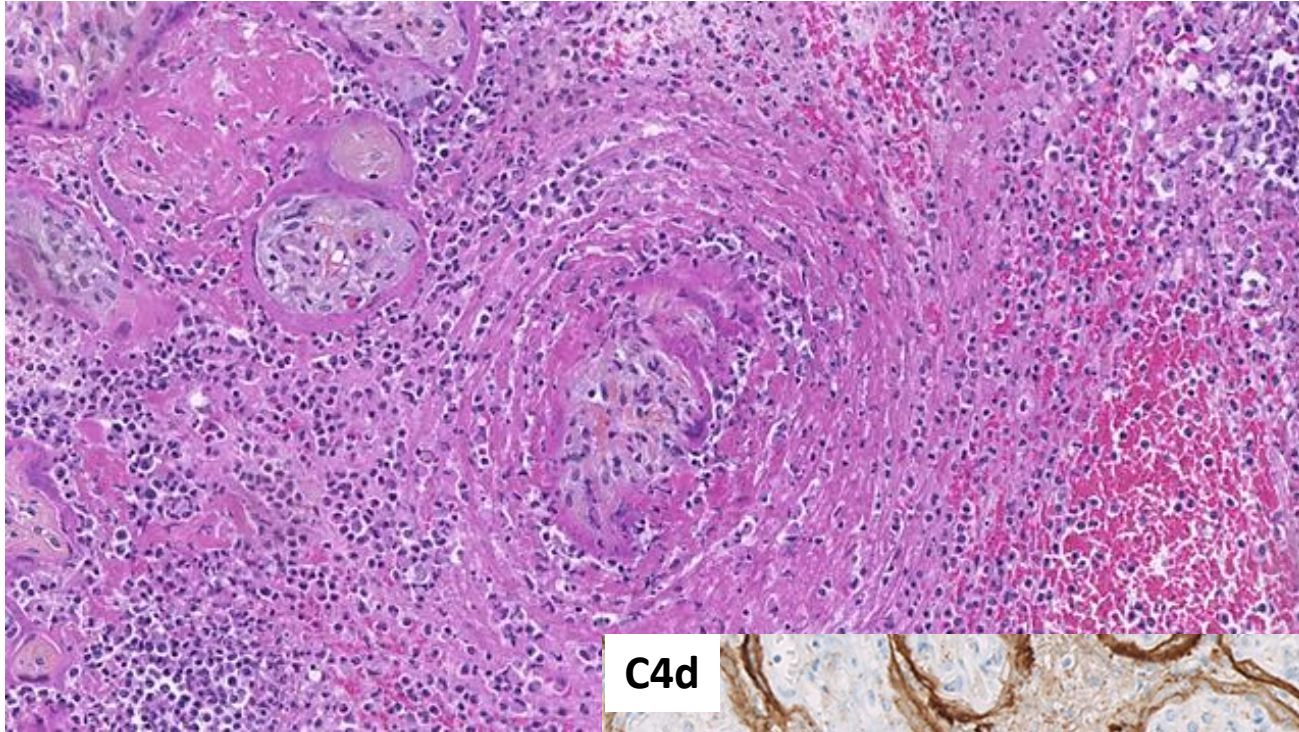


Placenta examination



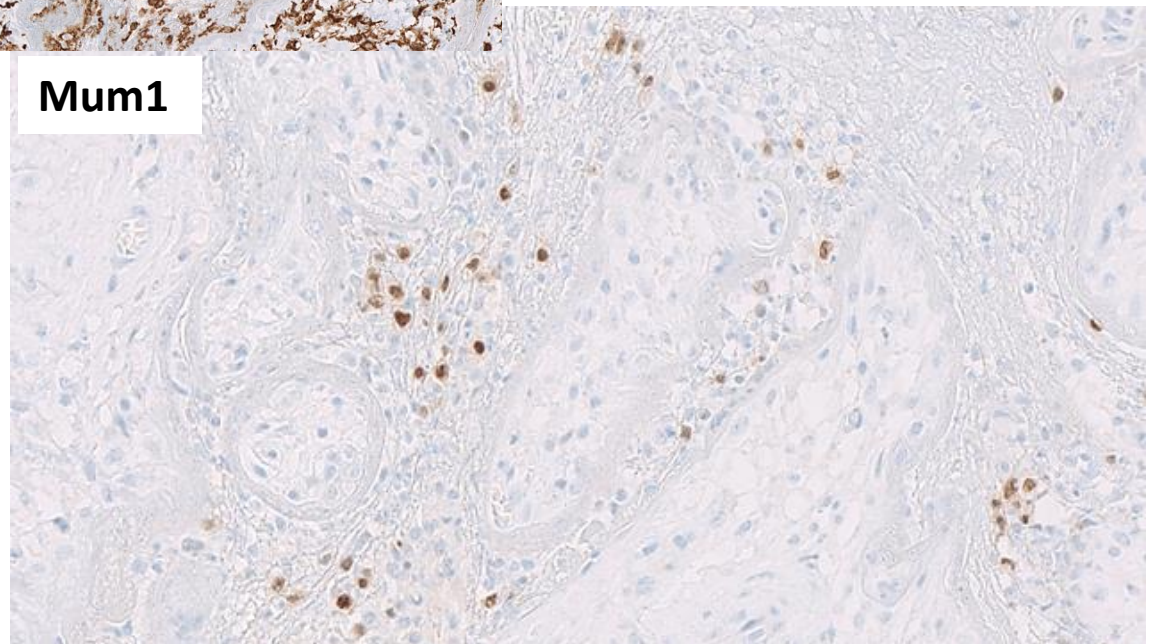
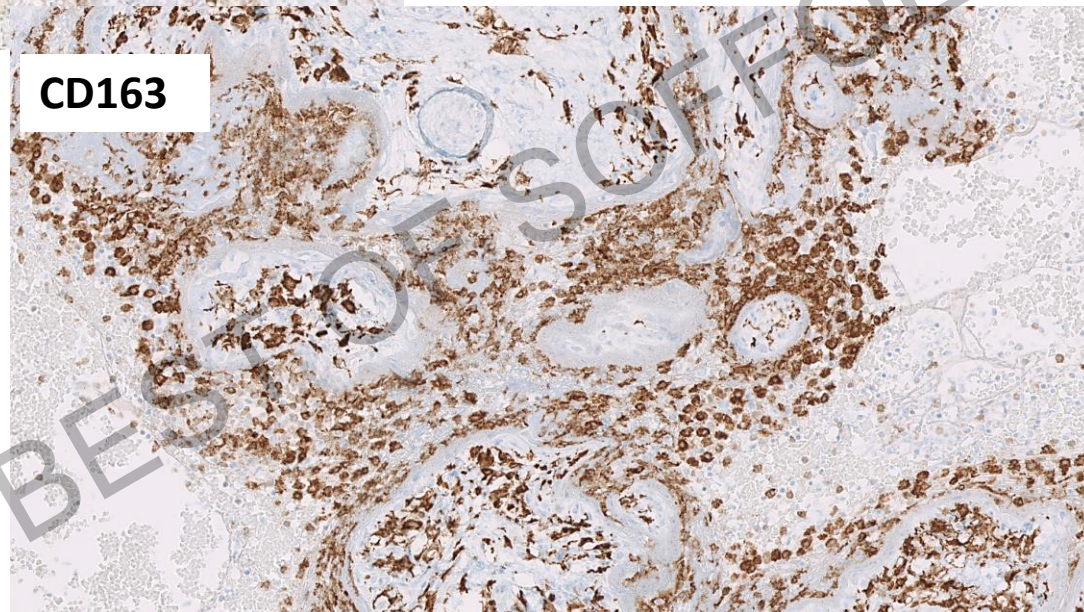
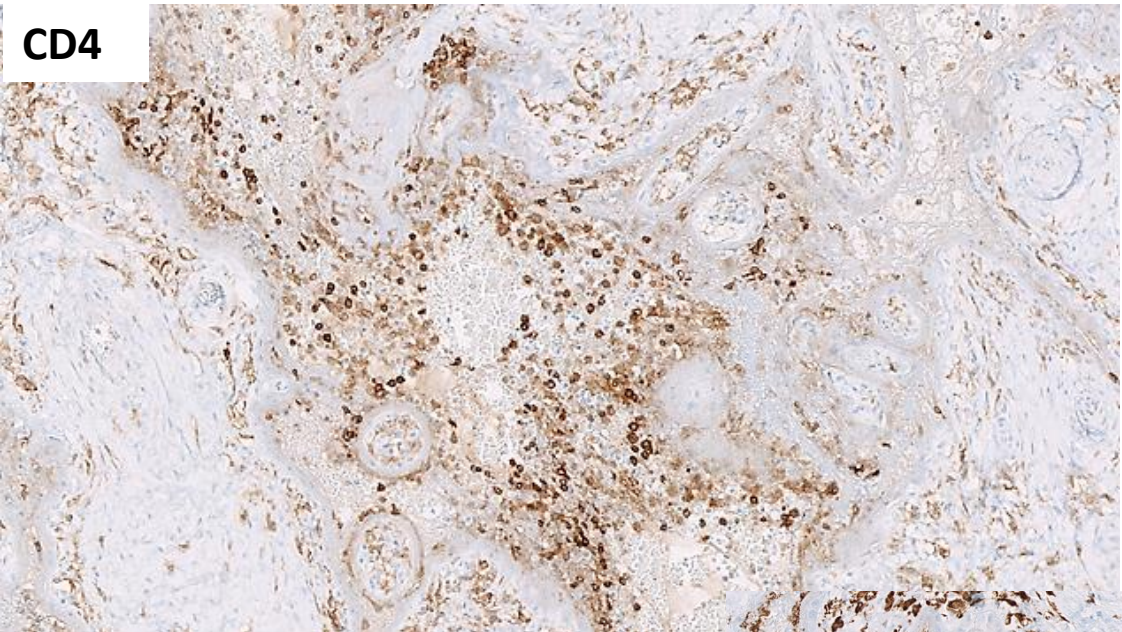
Macroscopic examination of the placenta revealed a diffusely a lattice-like deposition of fibrin (arrow) with a 6 cm sub chorionic thrombosis (asterix *) and multiple intervillous thrombosis (a). Normal macroscopic appearance of a placenta control at the same term as our case (24 WG).

Placenta examination

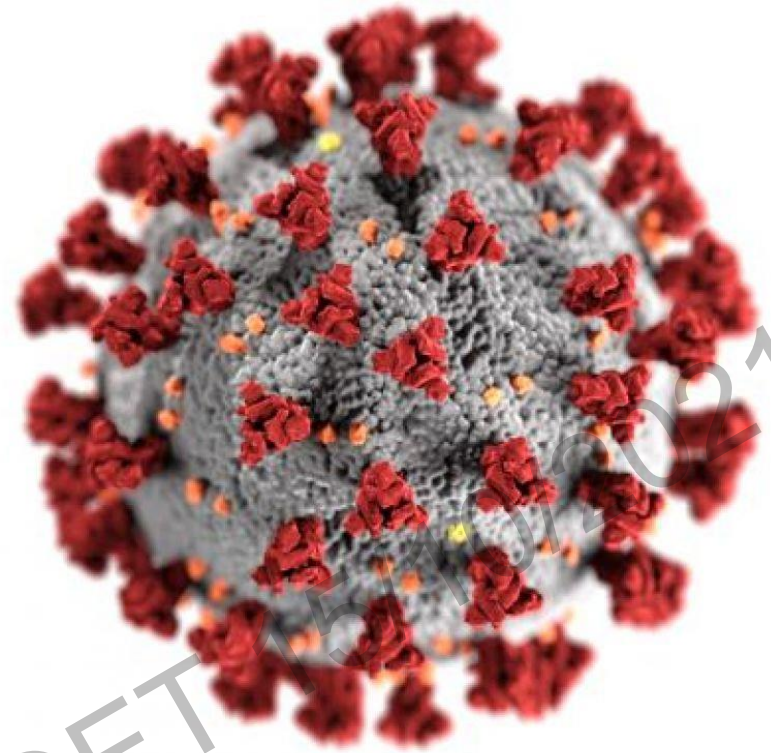
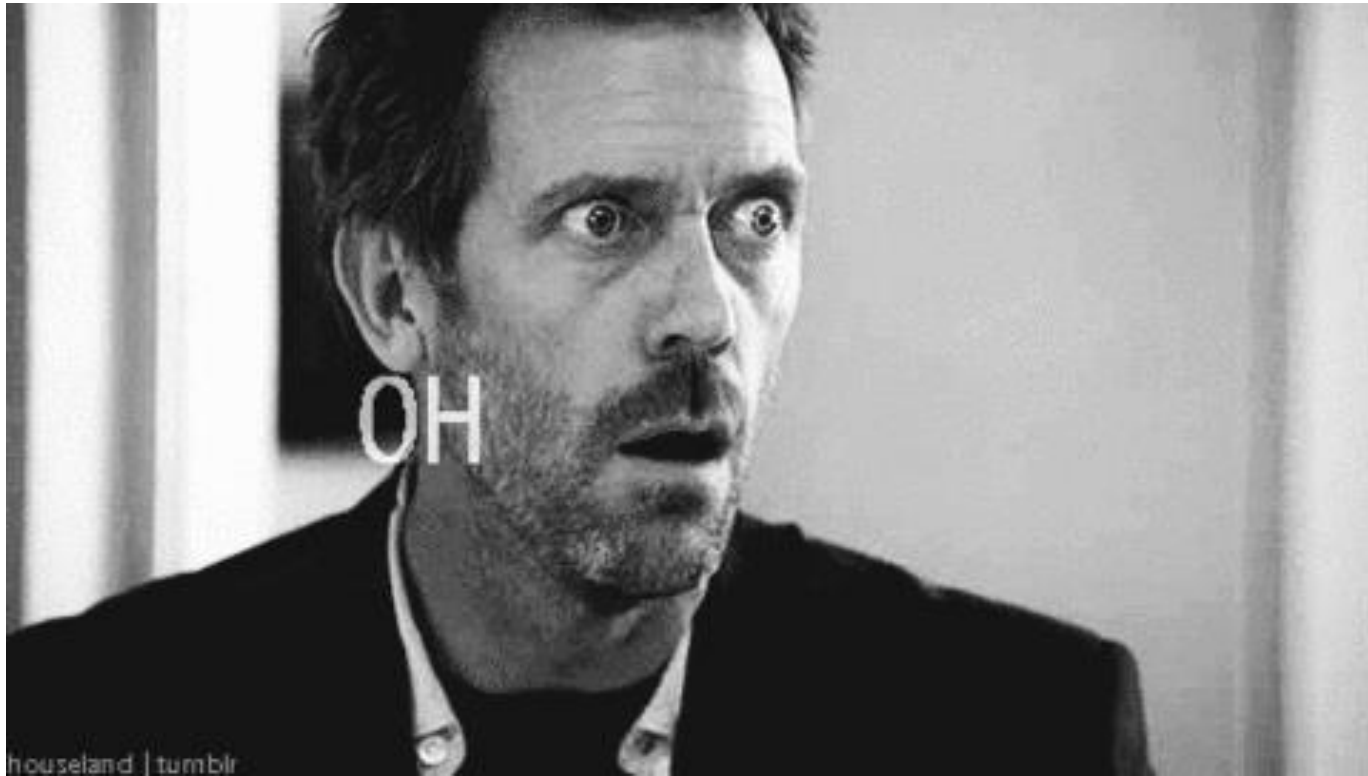


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Placenta examination



Journées BESUOLSOFFOET 15/10/2021

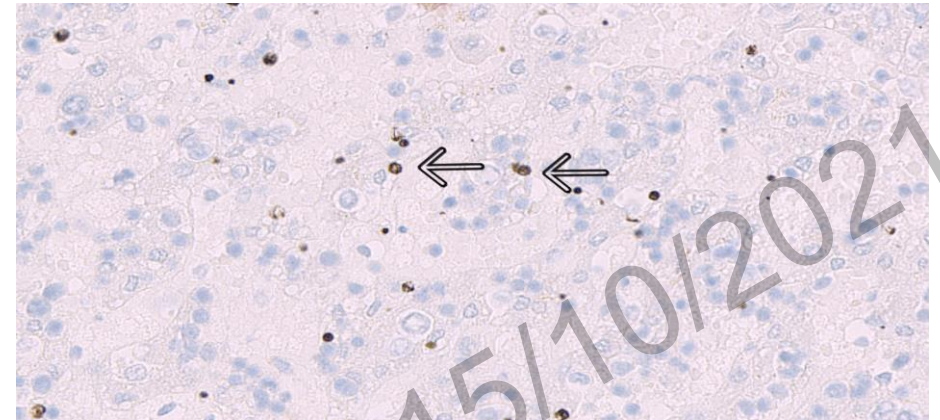
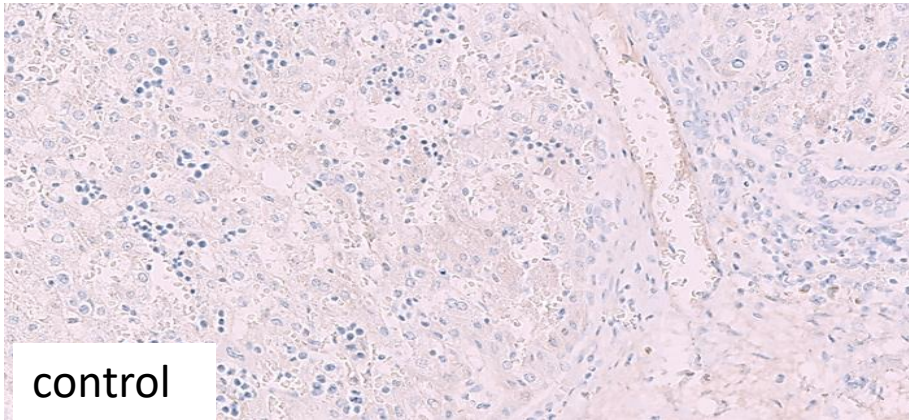


- 7 days before IUD: SARS-CoV-2 symptomatic infection in the mother (nasopharyngeal swab-RT-qPCR)
- Detection of the 20H/501Y. V2 (B1.351, Beta) variant.

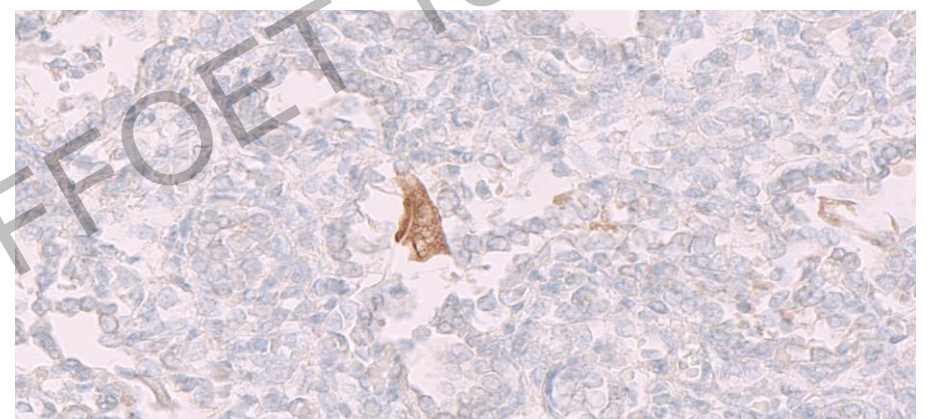
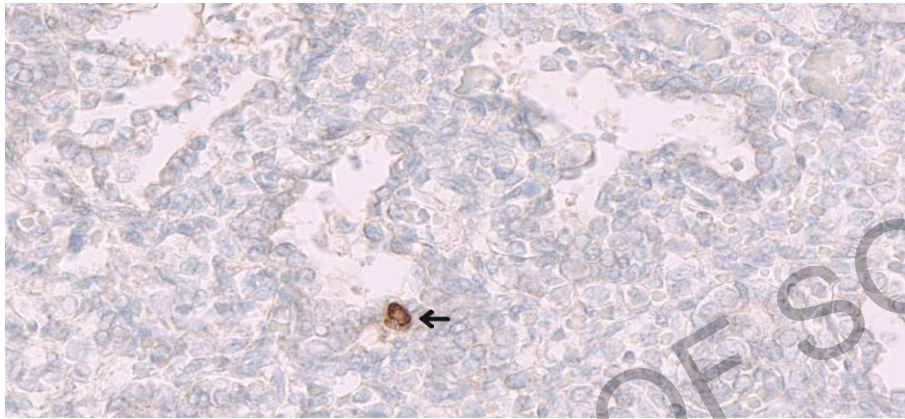
Fetal specimens

IHC SARS- CoV-2

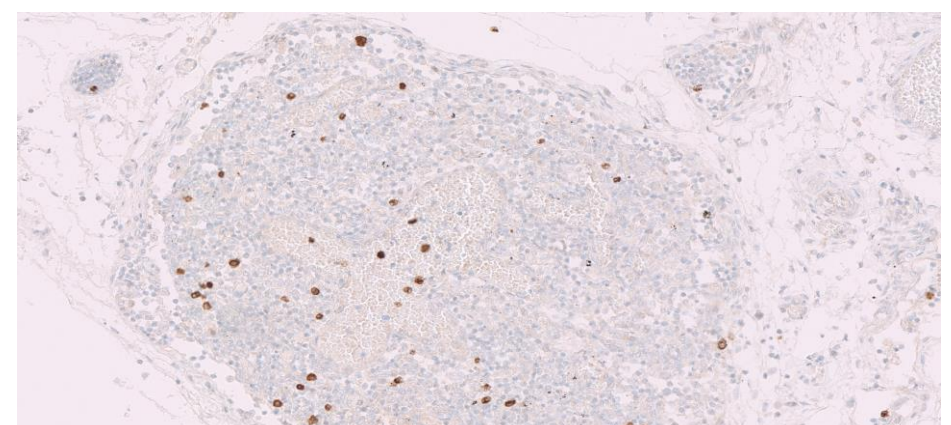
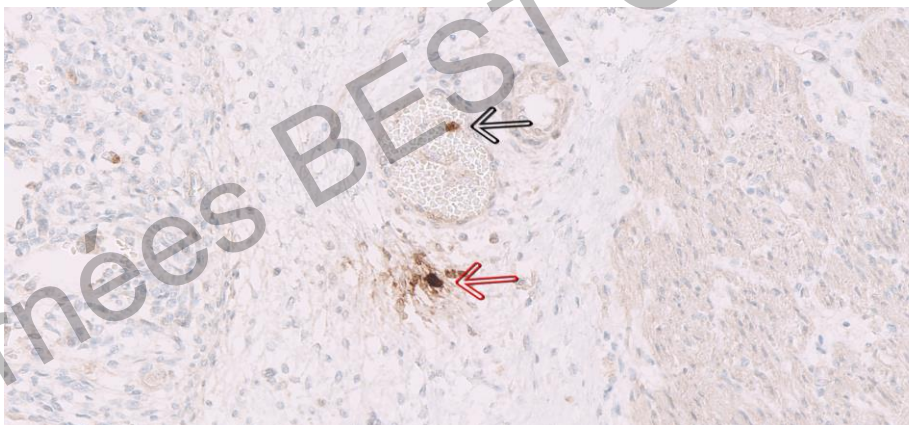
Liver



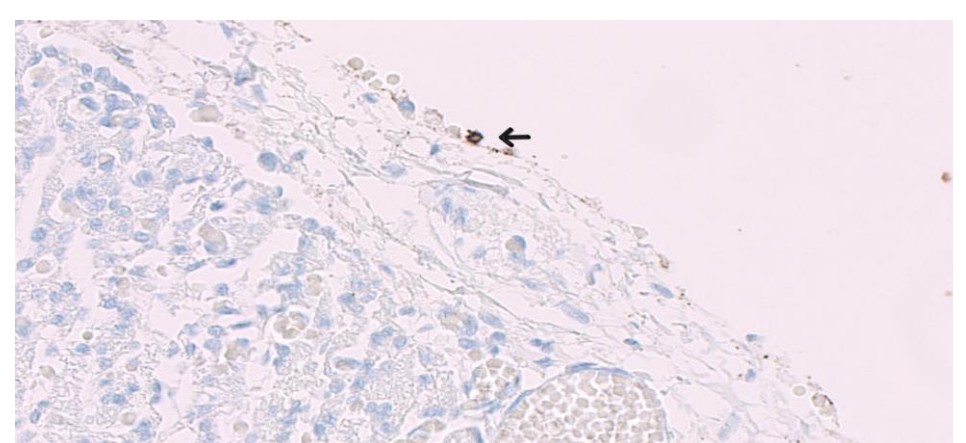
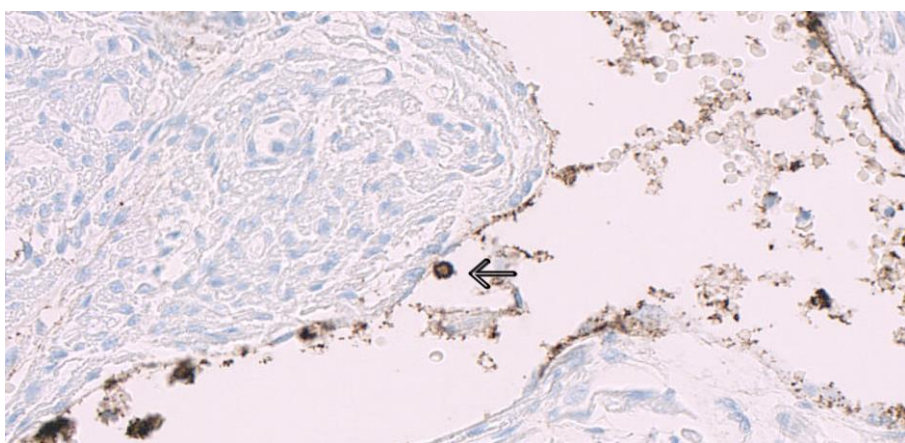
Lung



Stomach and
perigastric
lymph node



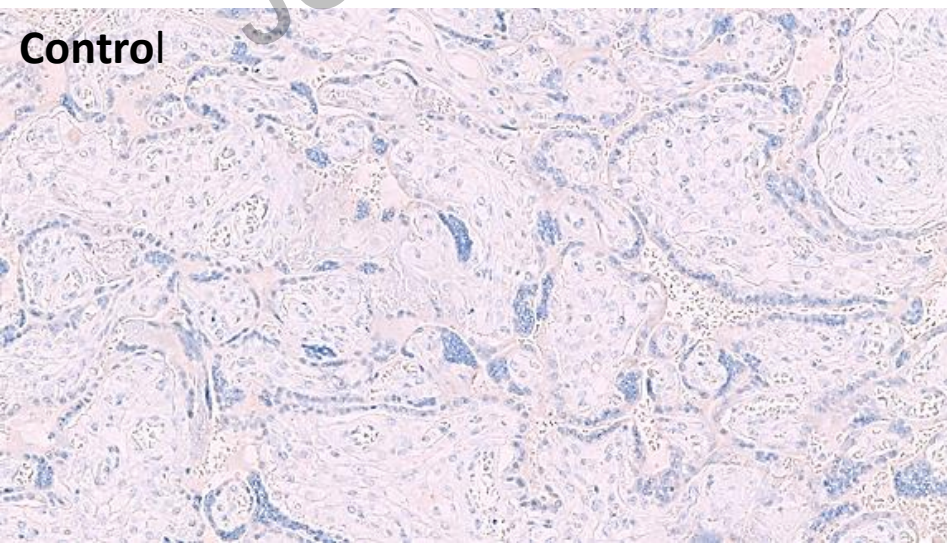
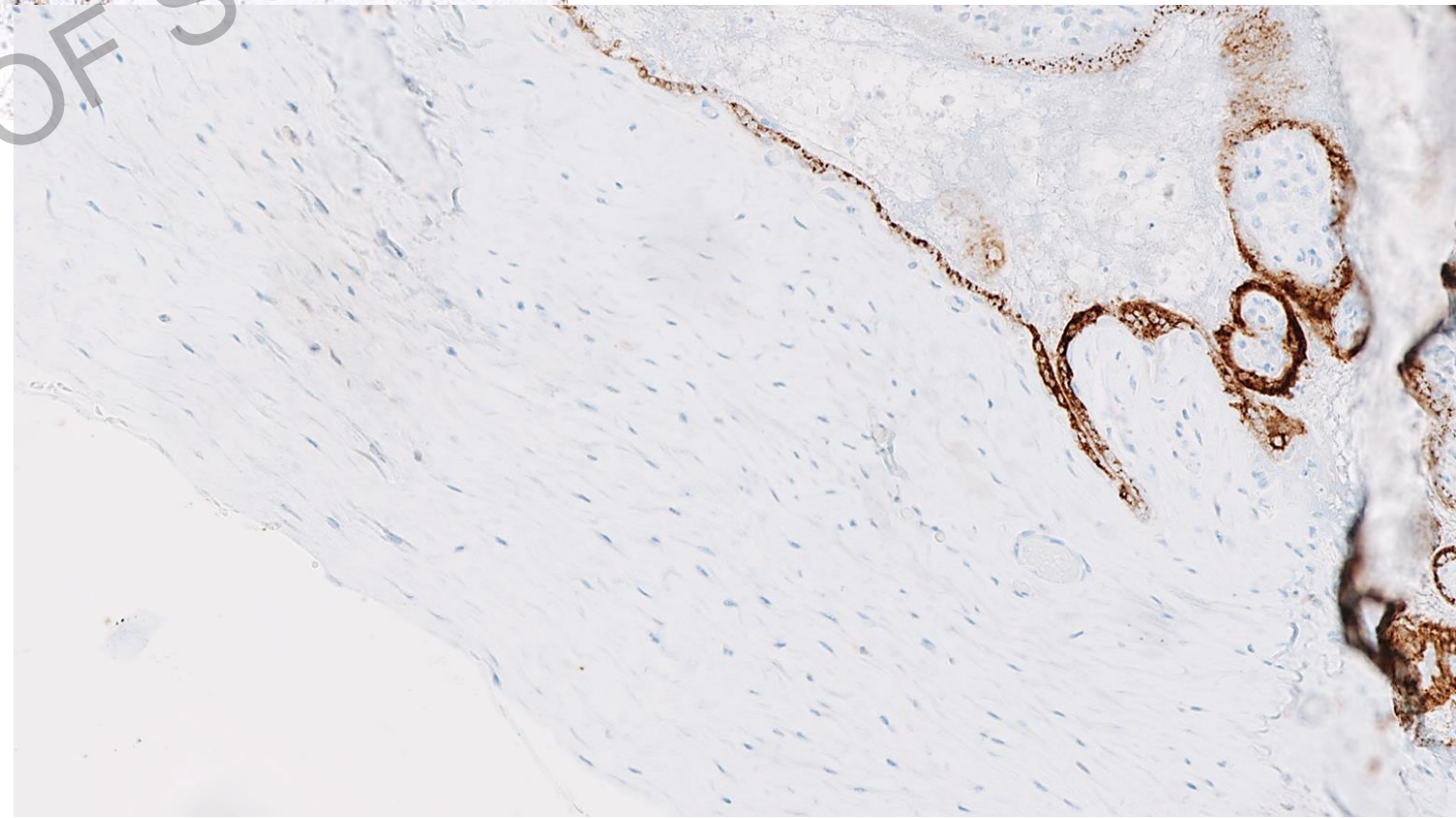
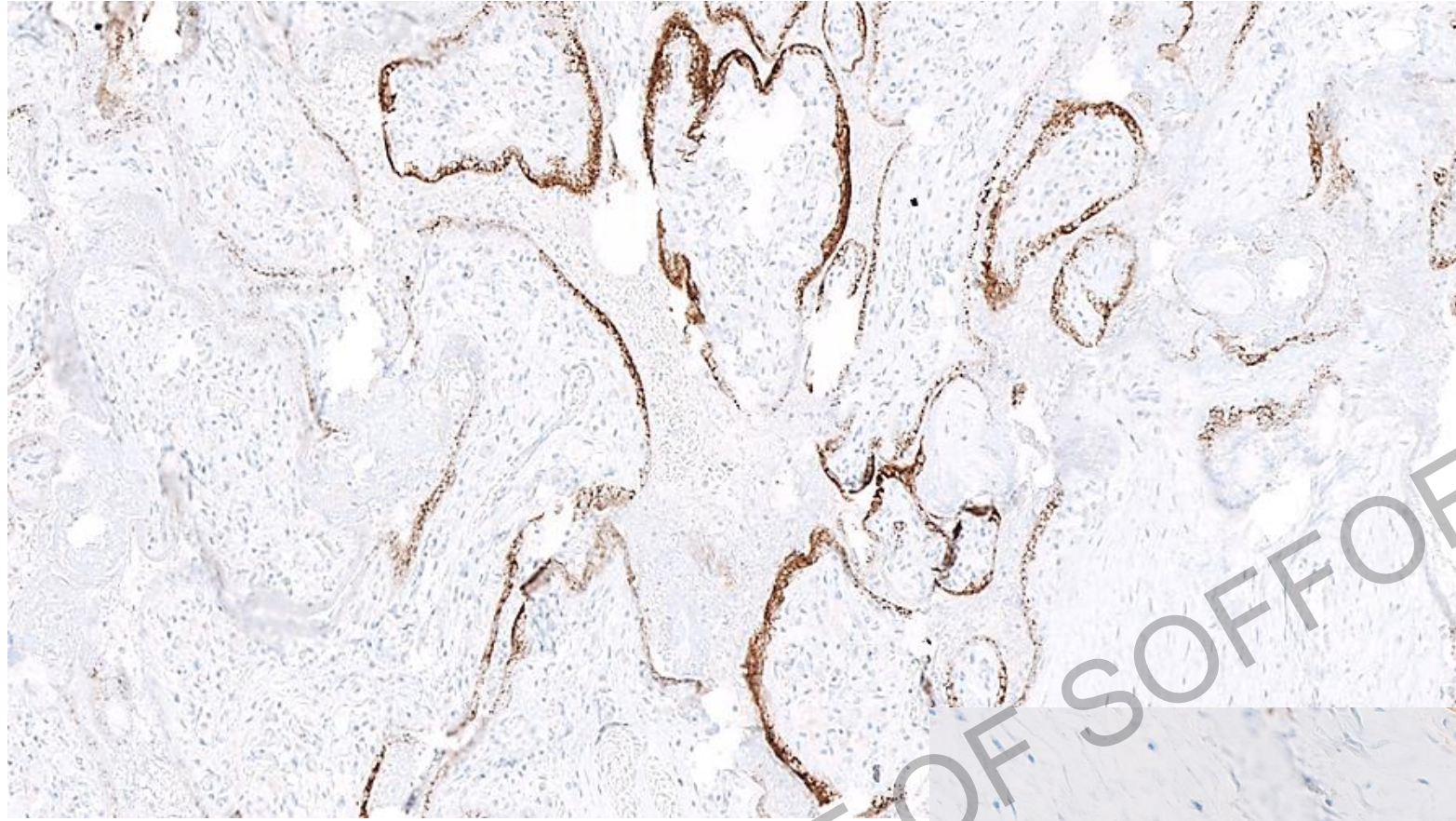
Heart



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Placenta

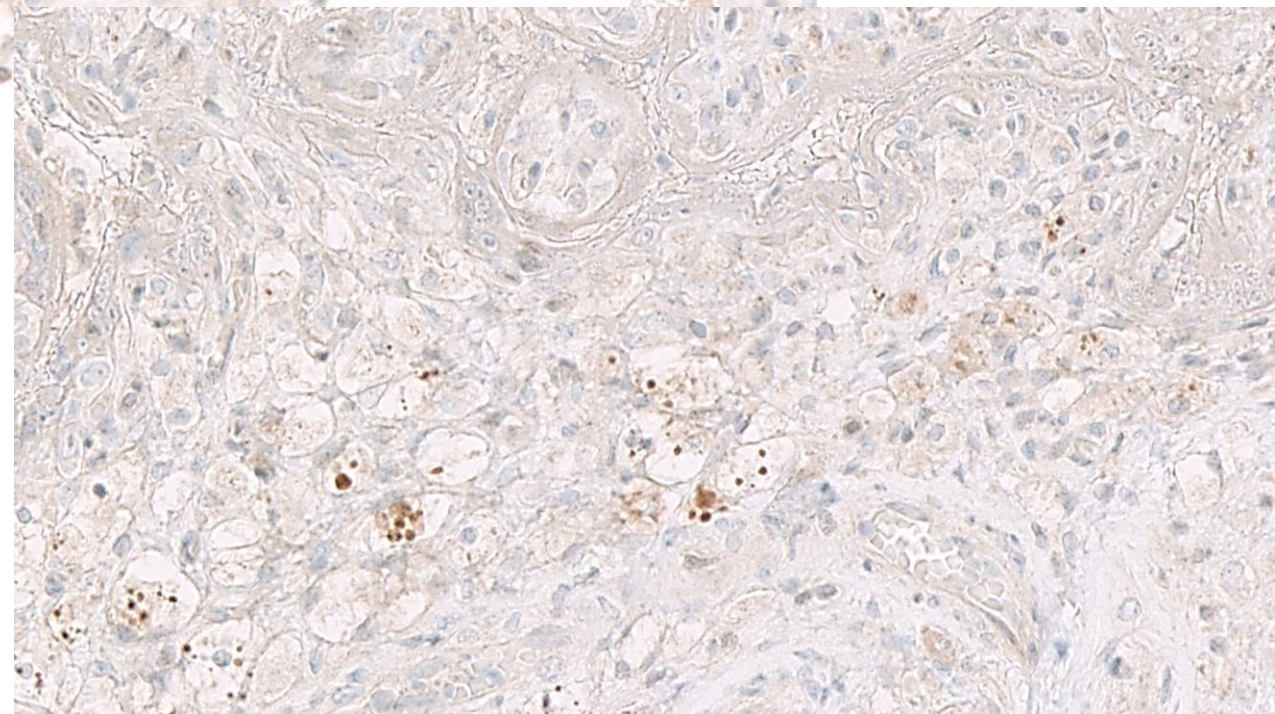
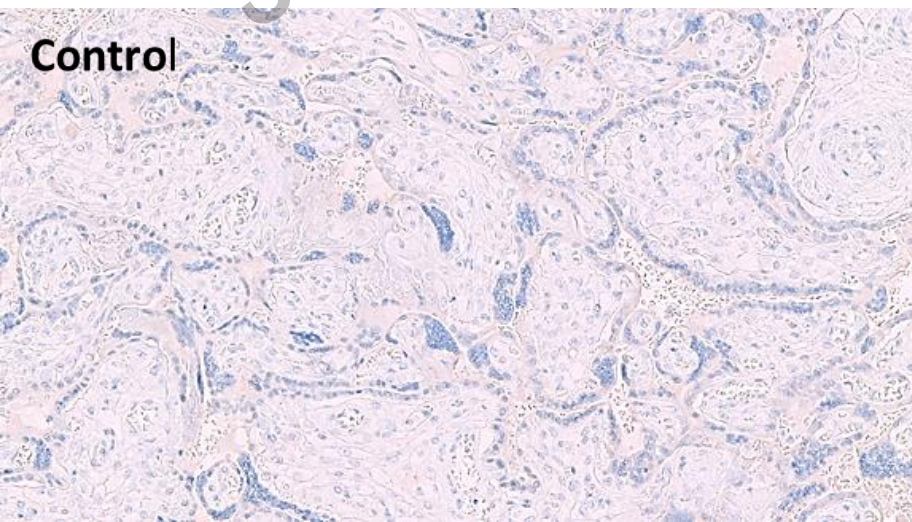
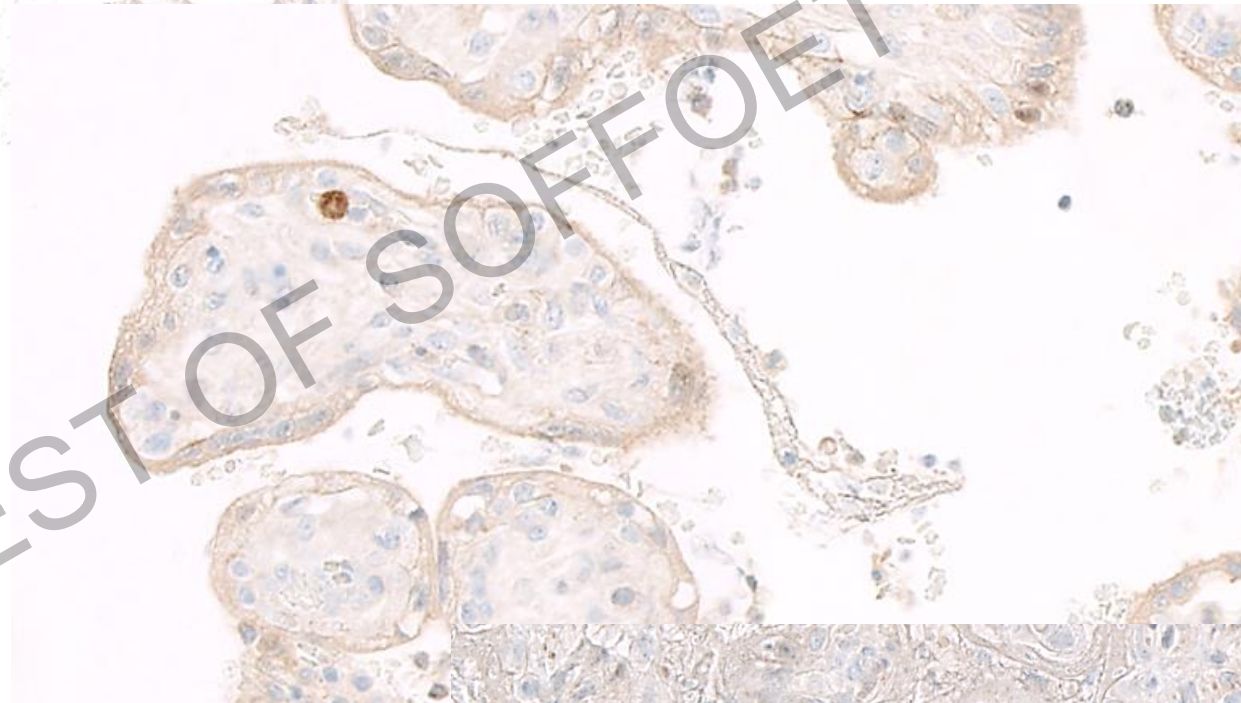
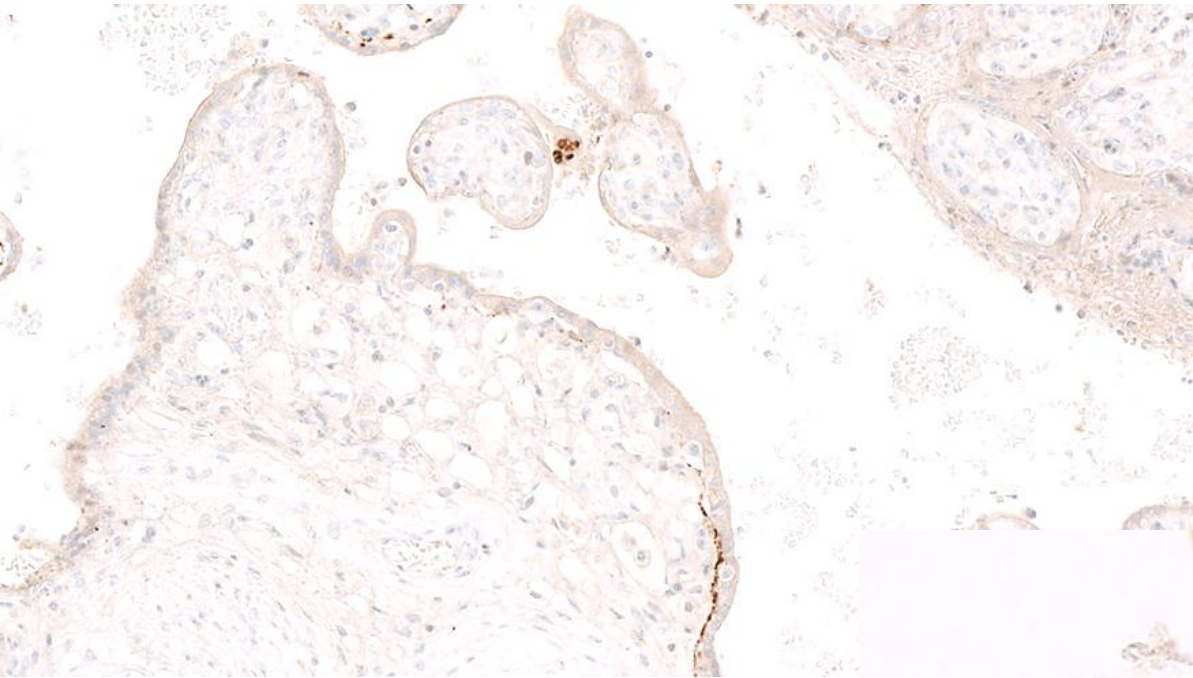
IHC SARS-CoV2 Spike protein



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Placenta

IHC SARS-CoV-2 envelope protein



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Fetal specimens

SARS- CoV-2 molecular testing

Sample		SARS-CoV-2 genome detection	
		RT-QPCR (ct)	RT-dPCR (status/positive droplet>4)
Fetal	Nasopharyngeal	+/33	NA
	Mouth	+/32,0	
	stomach	+	
	Bowel	-	
	anal	-	
Formalin fixed	Lung	+ / 34,6	+ / 8
	Liver	+ / 33	+ / 6
	Stomach	-	-
	Lymphatic node (perigastric)	NA	NA
	Heart	-	-
	Spleen	+ / 34,7	+ / 8
	Thymus	+ / 32,8	-
	Adrenal gland	-	-
	Kidney	-	-
Frozen tissue	Lung	+ / 35	+ / 21
	Stomach	-	NT
	Trachea	+ / 34,5	+ / 5
	Kidney	-	borderline/4

(“+” positive result ; “-“ negative result ; “NA” Tissue not available ; RT-QPCR : Real-time polymerase chain reaction ; RT - dPCR : Digital-Polymerase Chain Reaction).

Placenta

SARS-CoV-2 molecular testing

Sample		SARS-CoV-2 genome detection	
		RT-QPCR (<i>ct</i>)	RT-dPCR (<i>status/positive droplet</i> >4)
Formalin fixed	Extra placental membranes	+ / 33,8	NA
	Placental tissue	+ / 18,8 variant RT-PCR	+ / >20.000
Frozen tissue	Extra placental membranes	+ / 33,8	+ / 596
	Placental tissue	+ / 25,9	+ / >20.000

20H/501Y. V2 (B1.351, Beta) variant in-house real time reverse transcription-PCR assay

We concluded to a SARS-CoV-2 second trimester congenital infection with an IUD secondary to extremely diffuse placental injuries characteristic of a SARS-CoV-2 infection

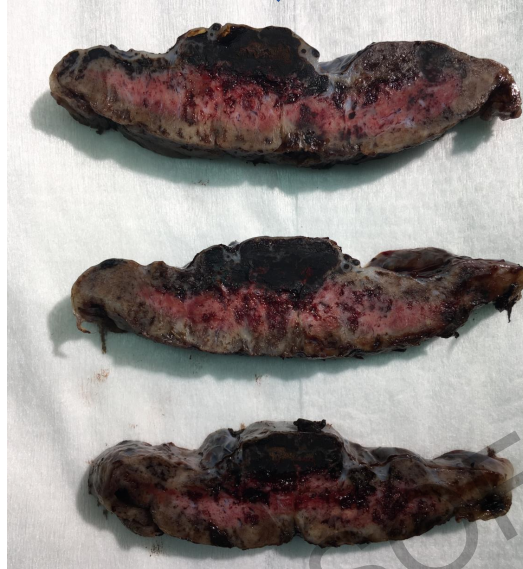
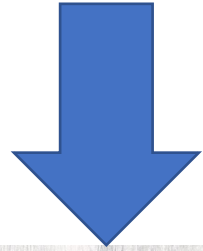
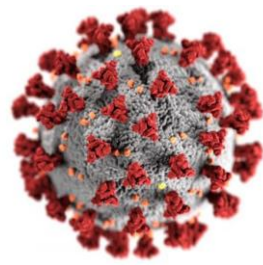
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Discussion

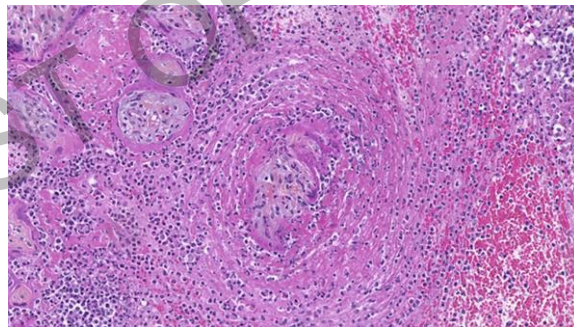
- Congenital infection *
- No indication for hospitalization one day before IUD!
- Thrombocytopenia: 4.24 x risk of patient mortality

*PS. Shah et al, *Acta Obstet Gynecol Scand.* 2020

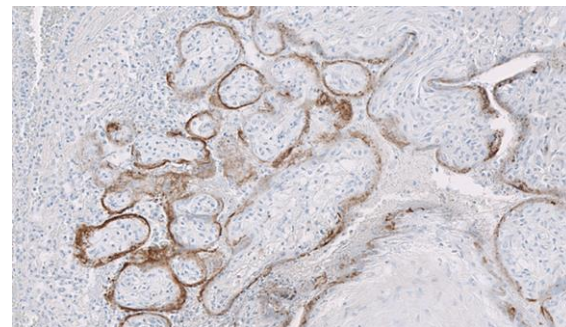
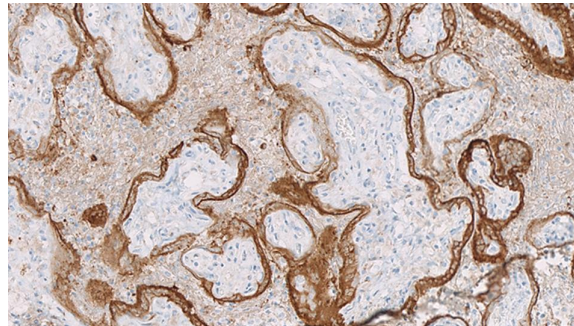
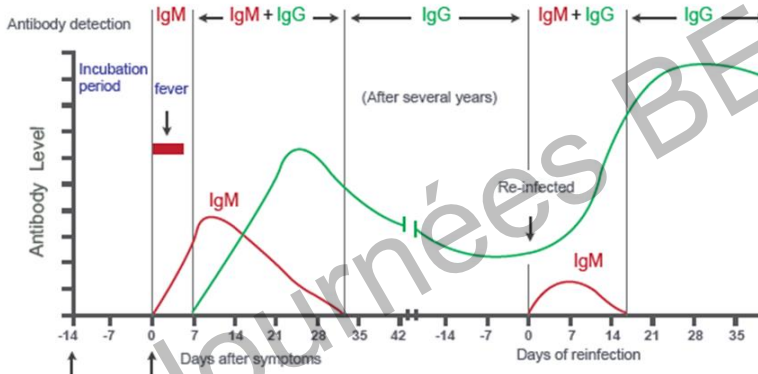
**Liu Y et al. *Platelets.* 2020 May



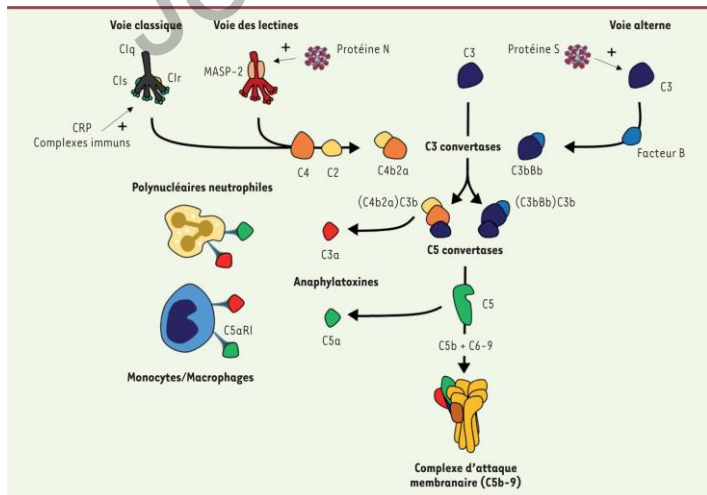
Placenta injuries → severely impaired maternal-fetal exchange

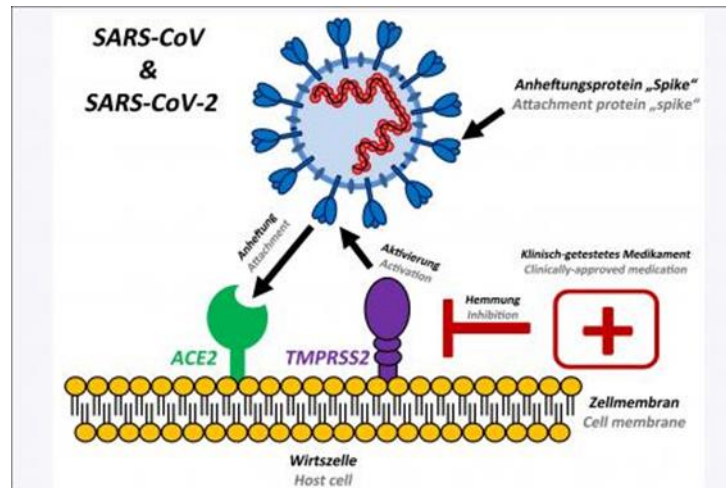
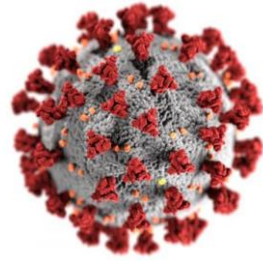


- CHIV & Trophoblaste necrosis → SARS-CoV-2 vertical transmission
- CD68, CD4 ?, Mum 1 (≈ CMV infection)



C deposition:
marker of progression of the disease
in pregnancy

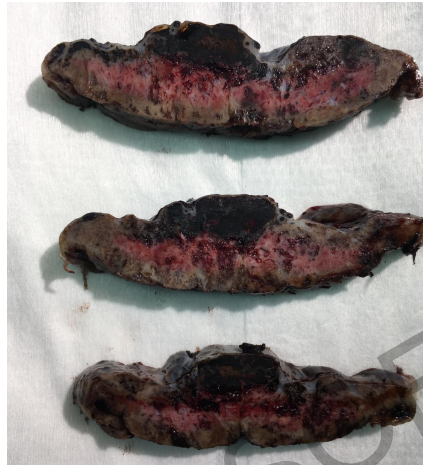
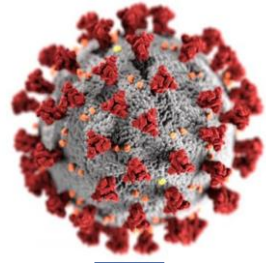




- VCT, VST, stromal and EVT cells, which express the ACE 2 gene
 - An increasing expression of ACE2 in EVT at 24 weeks
- EVT could play a major role of pathogenies of SARS-CoV2 infection on placental tissue at the second trimester.



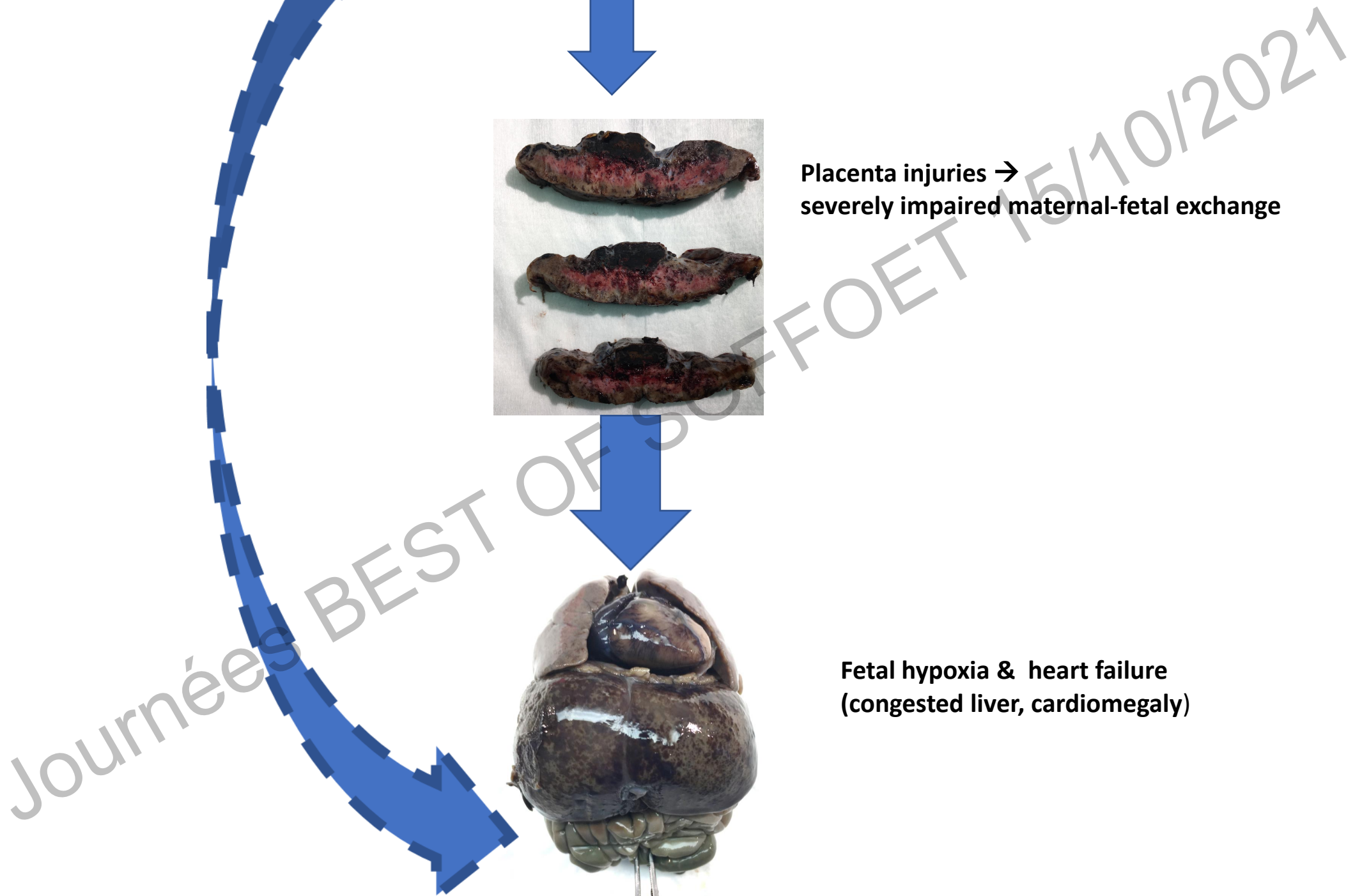
Placenta injuries →
severely impaired maternal-fetal exchange



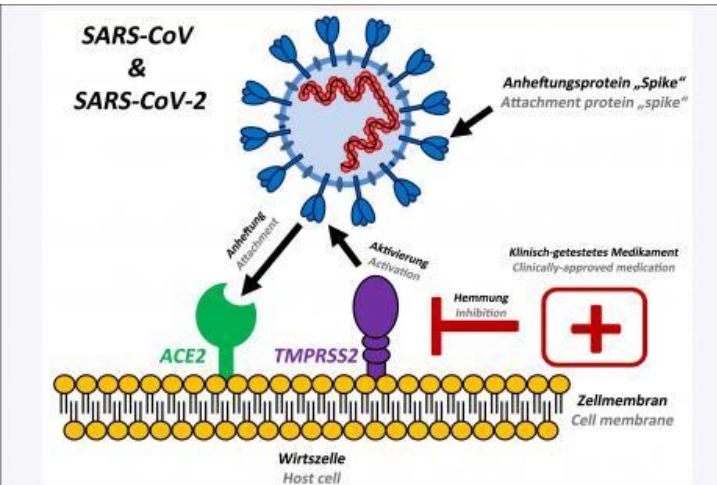
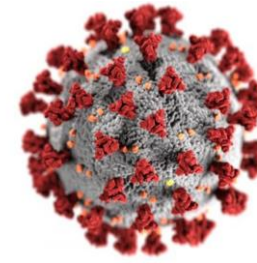
**Placenta injuries →
severely impaired maternal-fetal exchange**



**Fetal hypoxia & heart failure
(congested liver, cardiomegaly)**



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Heart (but cardiomyocytes testing of SARS-CoV2 (-))

Lung (alveolar-type cells)

≠ murine lung cell atlas (the late pregnancy stage to earliest post-natal days) : AirwayEpi>>AT1 et AT2
-> variability of ACE2 and TMPRSS2 expression on different lineage lung cells between the 2^{ed} and the last trimester ?

Liver (+)

Kidney: (-)



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CONCLUSION

We present a case of SARS-CoV-2 second trimester congenital infection, with IUD secondary to extremely diffuse placental injuries.

The involvement of certain variants in the poor prognosis of pregnancy outcome remains undetermined.

Emergency obstetrical management of pregnant women in cases of suspected vertical transmission of SARS-CoV2 should be considered, especially in the presence of reduced fetal movement with thrombocytopenia.

The
Economist



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