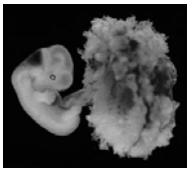
Erasmus MC
Universitair Medisch Centrum Rotterdam

Early pregnancy angiogenesis

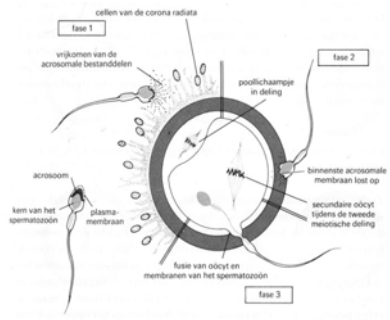
Niek Exalto



Varna 2008

Erasmus MC

Conception



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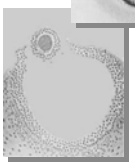
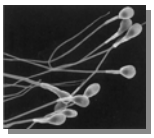
Abnormal karyotype

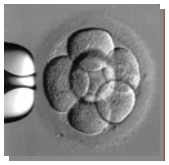
~ 26 %



~ 7 %



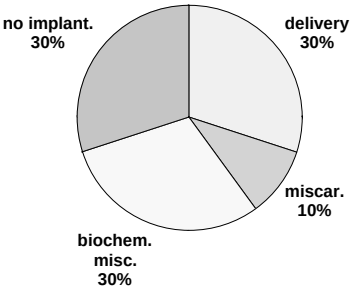
~ 40 %



Erasmus MC

Prognosis

Chart 1991 Baillière COG



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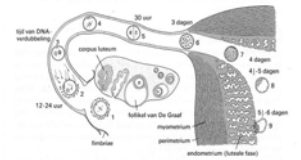
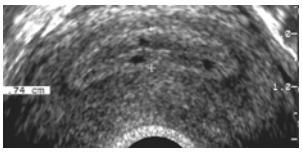
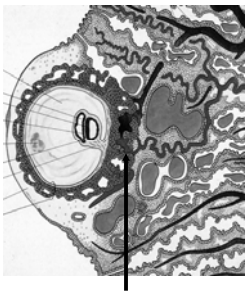
implantation

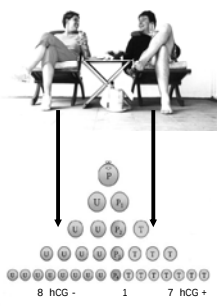


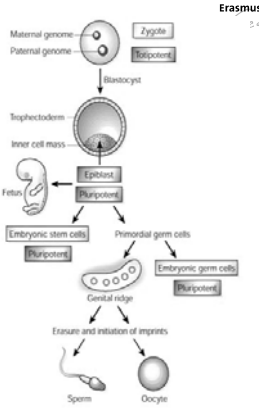




Erasmus MC

Imprinting





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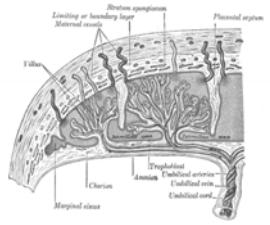
placenta



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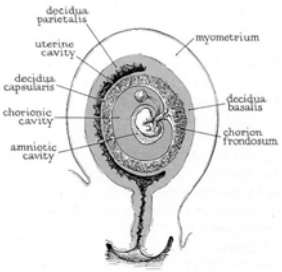
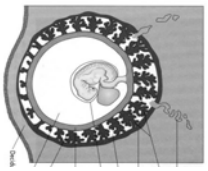
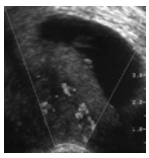
Intervillous space







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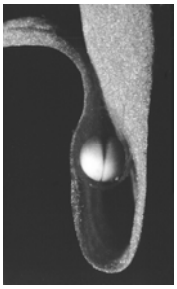
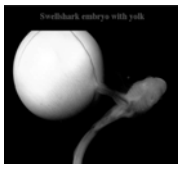
Evolution





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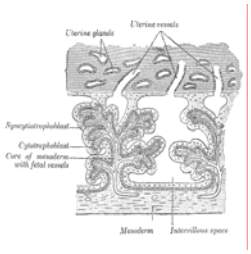
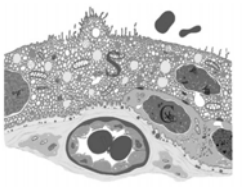
Vasculo-syncytial membrane





Erasmus MC

US vs chromosomal abn.

Minelli Ann Genet 1993

	Empty sac	Fetal death
Chromosomal abnormal	67 %	53 %
Trisomy	74 %	35 %
Trisomy 16 & 22	+	-
45XO	0 %	10 %

Erasmus MC

Chromosomal abnormalities

Geraedts 1999 Human Reprod

Trisomie	1	Lethal before implantation	
	16	only in miscarriages	
	13 and 18	survival	> 1 %
	21	survival	~ 20 %

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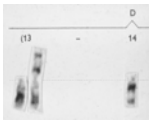
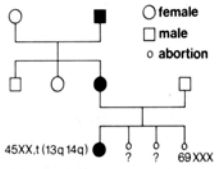
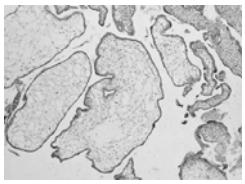
Case: 22 yrs, epilepsia recurrent miscarriage

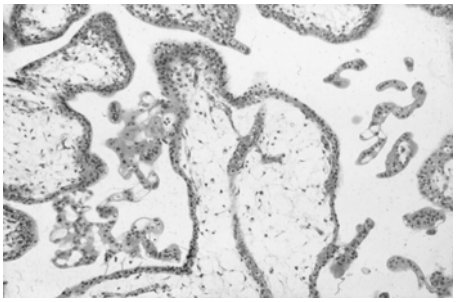






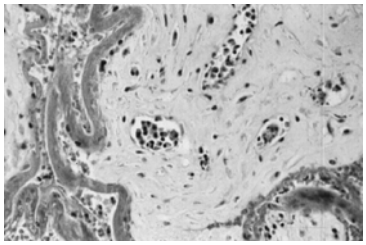
Erasmus MC

Normal vascularization



Erasmus MC

Retention time



Fibrosis

Trofobl deg

Vessels +++

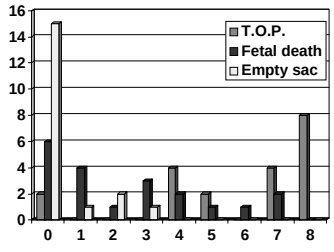
Retention time

Meegdes et al 1988 Fertil Steril

	< 15 dg	≥ 15 dg	Chi-sq
Number of misc. (%)	n = 8	n = 12	
vessels	6 (75)	7 (58)	ns
Fibrosis	1 (13)	9 (75)	p<0.05
Trophoblast deg	6 (75)	12 (100)	p<0.05
Hydropic deg	2 (25)	7 (56)	p<0.05

Vascularization

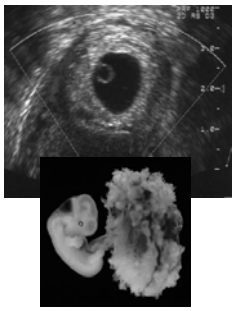
Meegdes et al 1988 Fertil Steril



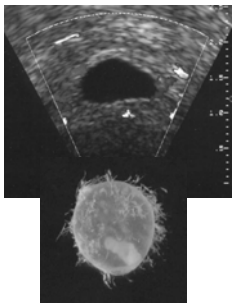
Gevascularized Villi	%
T.O.P.	89
Fetal death	26
Empty sac	9

Vascular desity of vascularized villi	
T.O.P.	17
Fetal death	5
Empty sac	4

normal

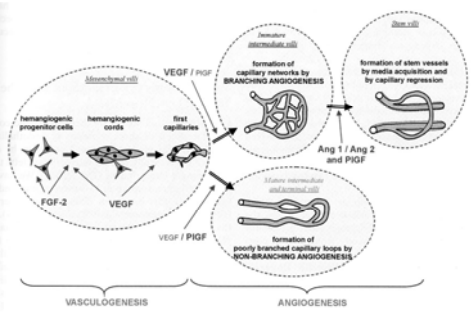


abnormal



Erasmus MC

Vasculogenesis ~ Angiogenesis



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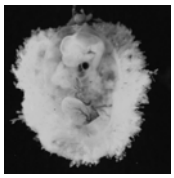
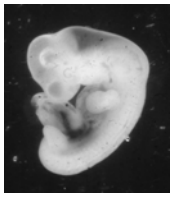
haematopoiësis

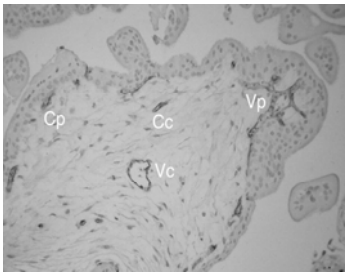
- Vessels have a lumen from 6 wk onwards
- In the beginning mainly nucleated blood cells
  - At 8 weeks only nucleated blood cells
  - between 10 and 12 weeks 10%
  - After 12 weeks sporadically





Erasmus MC

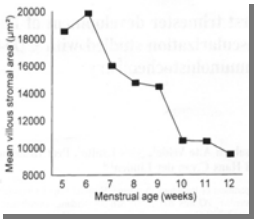
Vascular elements (CD 31)

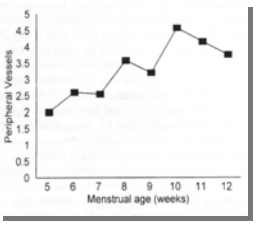


Erasmus MC

First trimester chrionic villi

te Velde et al. 1997 Human Reprod





Erasmus MC

Vascularisation in the first trimester

Lisman et al Fertil Steril 2002

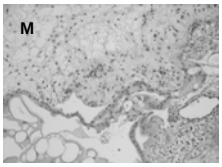
First trimester		cords		vessels		Total
	n	c	p	c	p	
Termiation of pregn.	12	1.5	1.6	(2.3)	(3.0)	8,4
Fetal death	12	(2.7)	0.6	0.6	0.9	4,8
Empty sac	12	(3.3)	0.6	0.6	0.2	4,7

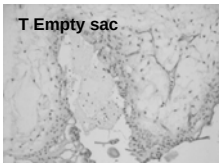
Abnormal development of vasculosyncytial membrane

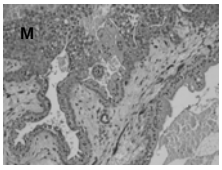
Erasmus MC

MOLA and Triploïdy

Lisman et al 2005 Human Reprod







Erasmus MC

Vascularisation in late miscarriage

Lisman et al 2002

16 - 22 weeks		cords		vessels	
	n	c	p	c	p
Normal	4	0.8	0.7	4.5	5.3
Chrom abn	10	2.5	2.7	3.2	2.7
IUGR	13	5.6	3.2	2.9	1.7

Erasmus MC

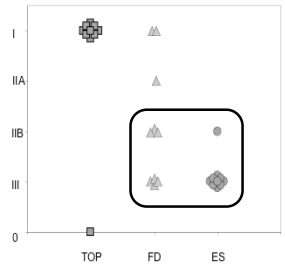
Vascularization Score (routine H-E)

Grade 0	insufficient number of villi
Grade I	Normal vessels centr. and peripherally in almost all villi (9/10)
Grade IIA	mild hypoplasia vessels less numerous and mainly centr. Not in all villi
Grade IIB	severe hypoplasia mainly avascular. Vessels present in a single villus
Grade III	Avascular all villi avasculair, sporadically a vessel

Erasmus MC

Classification

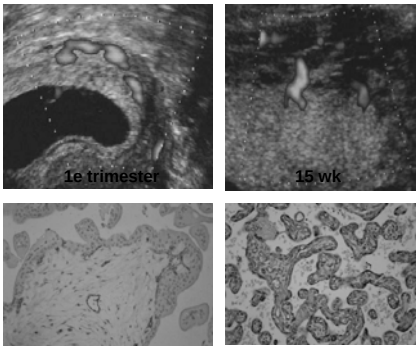
Hakvoort et al Human Reprod 2006



- Observers A,B,C & D
- 30 specimen
- Agreement 0.73 -0.90
- Kappa 0.64 - 0.86 (good - excellent)

Erasmus MC

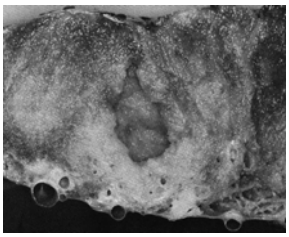
Flow



Erasmus MC

An anatomic basis for ultrasound images of the human placenta

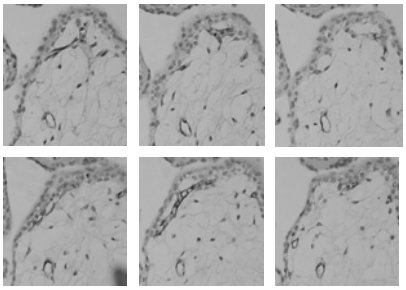
Vermeulen et al Am J Obstet Gynaecol 1985



Perfusion fixation
with formaldehyde
Art 70 mm Hg
Ven 20 mm Hg

Erasmus MC

3D reconstruction



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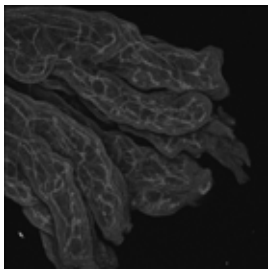
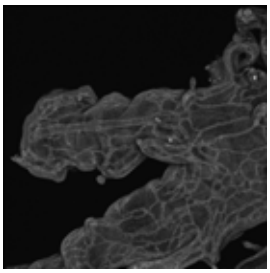
Confocal microscopy

6 wk

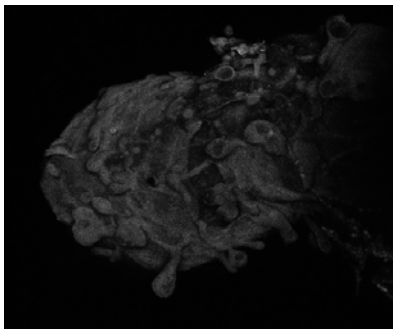


9 wk



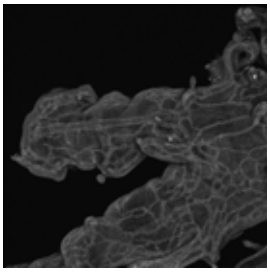
Erasmus MC

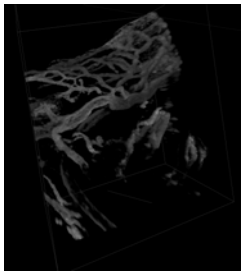
Mola



Erasmus MC

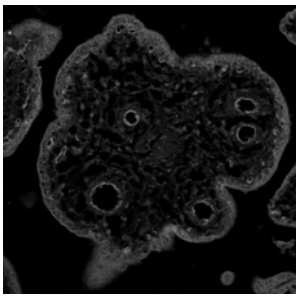
Confocal microsc => I-Space





Erasmus MC

Conclusie



Vascularization
- **Vasculogenesis**
- **Angiogenesis**

Absent (avascular)
- **empty sac**

Reduced development
- **fetal death**
- **growth retardation**

Vessels do not disappear
- **score 0 - III**